Postgraduate Medicine

Volume 29 · Number 4

APRIL · 1961

OFFICIAL JOURNAL OF THE INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

TABLE *of* CONTENTS

An Obstetric-Gynecologic Survey of the Problem of Perinatal Casualties
ROBERT E. L. NESBITT, JR., M.D. 333

Chronic Bronchitis and Pulmonary Emphysema
RICHARD V. EBERT, M.D. 341

Analgesic Agents for the Relief of Acute Pain
MAX S. SADOVE, M.D. AND M. J. SCHIFFRIN, PH.D. 346

Advances in Electrocardiography
DONALD C. OVERY, M.D. 352

Teaching of Medicine at the University of Washington With Emphasis on Endocrinology and Metabolism
ROBERT H. WILLIAMS, M.D. 415

PSYCHOSOMATIC MEDICINE—SPECIAL SERIES

Reactions of Medical Patients to Discharge or Threat of Discharge From a Psychosomatic Unit of a General Hospital
STANLEY M. KAPLAN, M.D. AND GEORGE C. CURTIS, M.D. 358

EMERGENCY SURGERY FOR GENERAL PHYSICIANS, PART 2

Anatomy for Surgeons
E. A. BOYDEN, PH.D. 365

Spontaneous Pneumothorax
J. BRADLEY AUST, M.D. 368

Traumatic Hemopneumothorax
SAMUEL W. HUNTER, M.D. 374

(Continued on page A-4)

Postgraduate Medicine is published monthly at Minneapolis, Minn., by IPMA Publishing Co., G. Victor Lowrie, executive vice-president; William H. Hull, professional relations manager; Muriel D. Ries, circulation manager; Fred Couzens, Eastern manager, 420 Lexington Ave., New York 17, N.Y., telephone Murray Hill 4-7752; Arthur G. Sullivan, Jr., Central-West manager, 203 North Cedar Street, Horicon, Wis., telephone Hunter 5-2003. Advertising representatives: McDonald-Thompson, 1008 Western Ave., Seattle 1, Wash.; 625 Market St., San Francisco 5, Calif.; 3727 W. 6th St., Los Angeles 5, Calif.; 2727 Oak Lane Ave., Dallas 19, Tex.; 3217 Montrose Blvd., Houston 6, Tex.; 620 Sherman St., Denver 3, Colo. Publication date: 10th of the month. Subscription rate $10.00 a year in the United States and Canada; $12.00 in foreign countries. Two volumes a year. Address all editorial and business correspondence to **Postgraduate Medicine**, Essex Building, Minneapolis 3, Minn., telephone Federal 9-8836. © 1961 by IPMA Publishing Co. Title Reg. U. S. Pat. Off. Second-class postage paid at Minneapolis, Minnesota and at additional mailing offices. Printed in U.S.A.

Tracheostomy in Traumatic Injuries
YOSHIO SAKO, M.D. 380

Traumatic Rupture of the Diaphragm
LLOYD D. MACLEAN, M.D. 383

SCIENTIFIC EXHIBIT

Radioautography in Gastric Cancer
N. B. ACKERMAN, M.D., A. S. MCFEE, M.D., B. T. SANTORO, M.D. AND O. H. WANGENSTEEN, M.D. 393

NUTRITION IN CLINICAL MEDICINE

Recent Experiences in Diagnosing and Treating Pernicious Anemia
WALTER G. UNGLAUB, M.D., AMOS L. PREVATT, M.D. AND GRACE A. GOLDSMITH, M.D. 399

CLINICAL STUDY

Clinical Evaluation of Fluphenazine in Cases of Anxiety and Other Psychoneuroses
TIBOR BODI, M.D., JOHN H. NODINE, M.D., PETER E. SIEGLER, M.D., HOWARD A. LEVY, M.D. AND JOHN H. MOYER, M.D. 408

CLINICOPATHOLOGIC CONFERENCE

Case Report
FROM THE VETERANS ADMINISTRATION HOSPITAL, HINES, ILLINOIS 423

SELF-HELP DEVICES

Homemaking: Kitchen Area; Storage Facilities
EDWARD W. LOWMAN, M.D. AND HOWARD A. RUSK, M.D. 431

POSTGRADUATE CLINICAL NOTES

156. Cancer of Female Genitalia 340
157. Basic Research 351

DEPARTMENTS

EDITORIALS 434

Suspended Judgment
Living Arrangements of the Aged
Institutionalized Population of Minnesota

(Continued on page A-6)

What does high "ABA" mean to you?

High serum levels of antibacterial activity mean fewer treatment failures in severe infections or in infections only marginally sensitive to penicillin. In other words, high "ABA" means . . .

consistently dependable clinical results

V-CILLIN K®

(penicillin V potassium, Lilly)

intense antibacterial activity

V-Cillin K produces greater antibacterial activity in the serum against the common pathogens than any other oral penicillin.[1-3]

unsurpassed safety

No form of penicillin has been shown to be less allergenic or less toxic than V-Cillin K.[4,5]

proved clinical effectiveness

Documented experience with penicillin V and potassium penicillin V reveals the clinical excellence of V-Cillin K.

Eli Lilly and Company
Indianapolis 6, Indiana, U.S.A.

133216

Now at lower cost to your patient

Prescribe V-Cillin K, in scored tablets of 125 and 250 mg., or V-Cillin K, Pediatric, in 40 and 80-cc. bottles.

References

1. McCarthy, C. G., and Finland, M.: Absorption and Excretion of Four Penicillins, New England J. Med., *263*:315, 1960. 2. McCarthy, C. G., Hirsch, H. A., and Finland, M.: Serum Levels after Single Oral Doses of 6-(α-phenoxypropionamido) Penicillanate and Penicillin V, Proc. Soc. Exper. Biol. & Med., *103*:177, 1960. 3. Griffith, R. S.: Comparison of Antibiotic Activity in Sera after the Administration of Three Different Penicillins, Antibiotic Med. & Clin. Therapy, *7*:129, 1960. 4. Editorial: New England J. Med., *263*: 361, 1960. 5. Editorial: New York J. Med., *60*:498, 1960.

FORTHCOMING FEATURES A-9

YOUR QUESTIONS ANSWERED A-20

Latent Syphilis

Headache Following Myelography

Obesity and Cryptorchism

Cancer of the Neck

Prolonged Bleeding and Dental Extraction

WHAT'S HAPPENING IN MEDICINE ..... Facing A-32-33

LABORATORY NOTES A-42

Photometers: Selection, Use and Maintenance

MYRTON F. BEELER, M.D.

FORENSIC MEDICINE A-60

A Law-Medicine Forum: Personality Disorders

OLIVER C. SCHROEDER, JR., LL.B., MORRIS M. KESSLER, M.D. AND EDWARD J. SCHIFF, M.D.

MEETINGS AND POSTGRADUATE COURSES A-69

RADIOLOGY FOR PRACTICING PHYSICIANS A-79

Beryllium Disease

PAUL C. HODGES, M.D.

THE EDITOR'S MAIL A-84

MEDICINE FROM ABROAD A-90

NEW FOR YOUR ARMAMENTARIUM A-108

GREAT NAMES IN AMERICAN MEDICAL HISTORY A-114

Austin Flint, Sr., M.D., New York

YOUR FINANCES

Financial Planning for the Medical Practitioner A-123

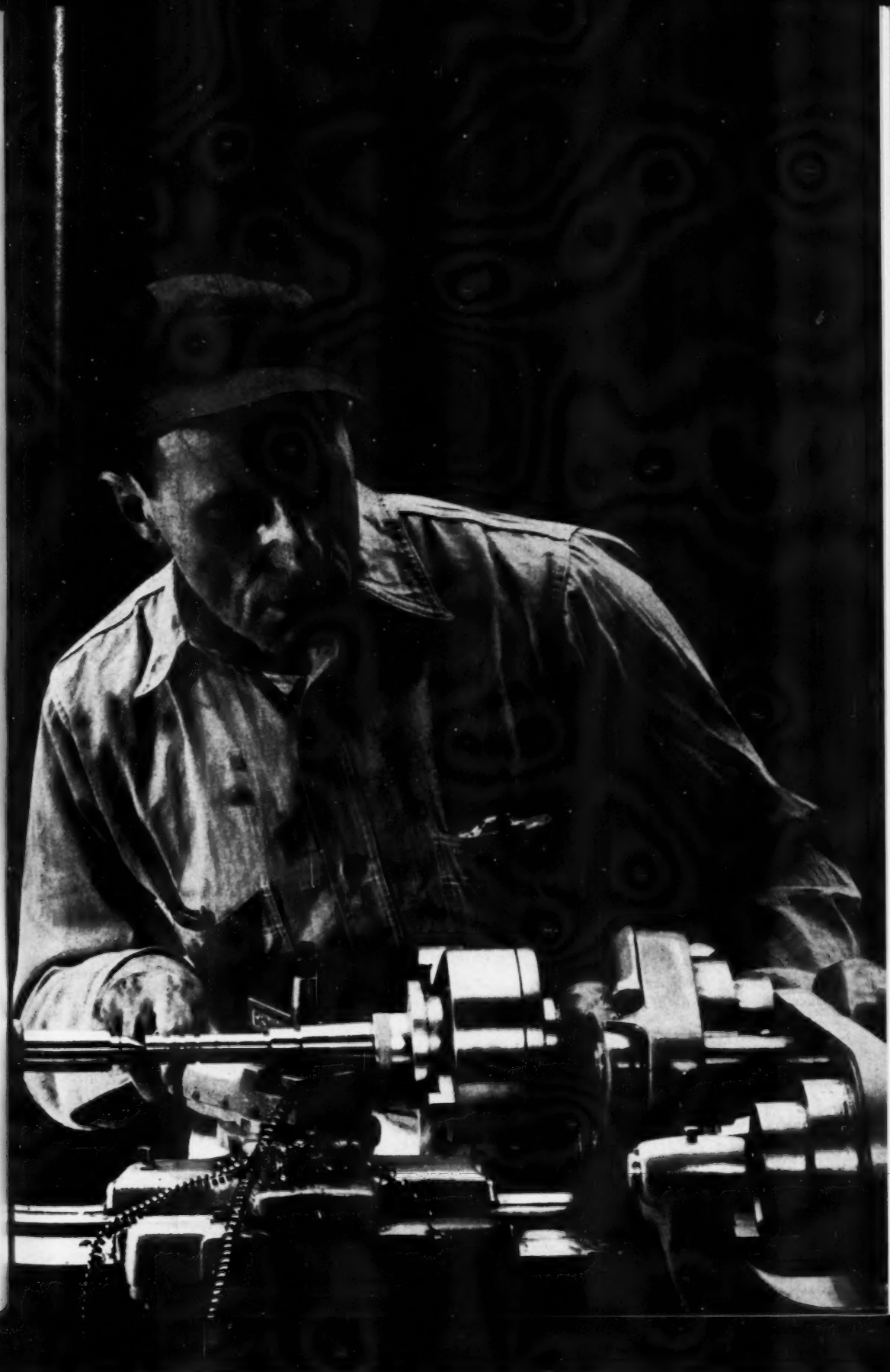
PRODUCTS BY THERAPY INDICATIONS A-139

THE MEDICAL BOOKMAN A-148

DR. PEPYS' PAGES. Morris Fishbein, M.D. A-162

THE MEDICAL MUSE. Richard Armour A-166

INDEX TO TECHNICAL EXHIBITS A-174



Your Questions answered

Readers may send questions from their own practice or other medical problems which will be answered by qualified consultants. Replies are forwarded by mail immediately and selected questions and answers are published each month in this section.

• LATENT SYPHILIS

Q. A 24 year old man has early latent syphilis. Results of the *Treponema pallidum* immobilization test were positive; however, spinal-fluid tests gave negative results, and a physical examination revealed no abnormalities.

Eight months ago this patient received 10 shots from another physician. What further treatment would you suggest?

M.D.—Maine

A. Since the type of shots the patient previously received is not specified, this case must be approached as if no treatment at all had been given. I would recommend that the patient receive 600,000 units of procaine penicillin G every day for six days, the total dosage being 3,600,000 units. This dosage should be repeated in a year.

• HEADACHE FOLLOWING MYELOGRAPHY

Q. A patient has had headaches more or less continuously since 1957, when a myelogram was done in which PANTOPAQUE® was used. Injection was made at the second lumbar segment. Approximately 1 cc. of residual contrast medium was noted in x-rays taken later.

Several years ago, I had another patient who had somewhat the same experience. What causes headaches following this procedure?

M.D.—Pennsylvania

A. It is true that some patients have had headaches after myelography; however, many hundreds of patients have not complained of this symptom following myelography with Pantopaque, even though oil has remained in the subarachnoid spaces. It is difficult to discern any definitive relationship between the myelogram, the retained oil and the occurrence of headaches.

• OBESITY AND CRYPTORCHISM

Q. A nine year old boy of above-average intelligence has a form of cryptorchism in which the scrotum usually is not filled out except when intraabdominal pressure is increased, as on bending, sneezing and deep respiration. At such times both testes descend and are of normal size, shape and consistency. Recently, fatty deposits have appeared on the external genitalia. The chest and buttocks measure 77 cm. and 86 cm. respectively; the boy weighs 102 lb. and is 4 ft. 5 in. tall. Slight genu valgum and lordosis also are present.

What treatment would you suggest for this patient?

M.D.—Sudan

A. The boy apparently is very much overweight, even considering the somewhat normal obesity of the preadolescent. His height falls in the fiftieth percentile, which is average for his age, but his weight is well above the ninety-seventh percentile, or a surplus of some 30 lb. It would be interesting to know if the bone age is advanced.

The fact that the testes descend with increased intraabdominal pressure and are of normal size and consistency is most reassuring. Since increased gonadotropic secretion can be expected in the next few years, permanent descent and maturation of the testes should occur. Unless there is accompanying herniation, surgery is contraindicated. From the information given, it appears that this boy is normal except for excessive obesity.

(Continued on page A-22)

"...extraordinarily effective diuretic..."[1]

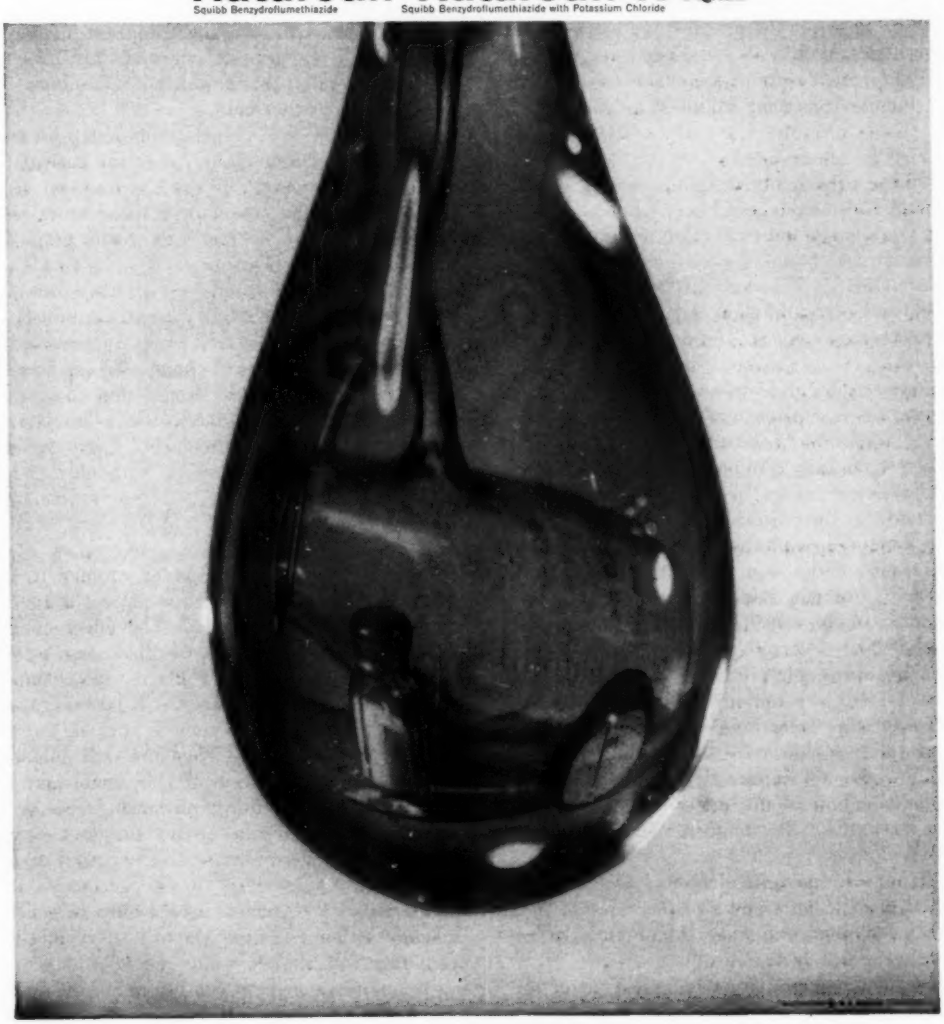
Efficacy and expanding clinical use are making Naturetin the diuretic of choice in edema and hypertension. It maintains a favorable urinary sodium-potassium excretion ratio, retains a balanced electrolyte pattern, and causes a relatively small increase in the urinary pH.[2] More potent than other diuretics, Naturetin usually provides 18-hour diuretic action with just a single 5 mg. tablet per day — economical, once-a-day dosage for the patient. Naturetin c̄ K — for added protection in those special conditions predisposing to hypokalemia and for patients on long-term therapy.

Supplied: Naturetin Tablets, 5 mg., scored, and 2.5 mg. Naturetin c̄ K (5 c̄ 500) Tablets, capsule-shaped, containing 5 mg. benzydroflumethiazide and 500 mg. potassium chloride. Naturetin c̄ K (2.5 c̄ 500) Tablets, capsule-shaped, containing 2.5 mg. benzydroflumethiazide and 500 mg. potassium chloride. For complete information consult package circular or write Professional Service Dept., Squibb, 745 Fifth Avenue, New York 22, N. Y.

References: 1. David, N. A.; Porter, G. A., and Gray, R. H.: Monographs on Therapy 5:60 (Feb.) 1960. 2. Ford, R. V.: Current Therap. Res. 2:92 (Mar.) 1960.

Naturetin Squibb Benzydroflumethiazide **Naturetin c̄ K** Squibb Benzydroflumethiazide with Potassium Chloride

SQUIBB



• CANCER OF THE NECK

Q. A 49 year old white man had anaplastic scirrhous cancer of the neck. The first symptom noted was asymptomatic swelling of the right side of the neck. The site of the primary cancer is unknown, but it may be in the right carotid sinus. There have been repeated metastases to the ribs.

Roentgenographic examination of the sinuses and barium studies of the upper and lower gastrointestinal tract yielded normal findings. Rectal and proctoscopic examination did not reveal any abnormalities.

The patient has had a complete resection of the neck, including the arteries, jugular vein and lymph nodes. He has also received x-ray therapy. Since the primary site of the cancer is unknown, what further treatment would be advisable?

M.D.—Ohio

A. In the presence of distant metastases to the ribs and presumably elsewhere, the only treatment would be radiation therapy for local symptomatic sites or, possibly, systemic chemotherapy. As the patient is followed, the primary site may become evident, and the therapy would then change to management of the specific problem presented.

Metastases in cervical lymph nodes cannot be managed on an entirely rational basis unless the primary tumor is demonstrable. The location of the metastases may give a clue as to the primary site. Metastatic nodes in the upper neck, with other nodes in the posterior neck triangle, usually occur with a nasopharyngeal primary tumor. Subdigastric nodes containing metastatic squamous-cell carcinoma usually occur with primary carcinoma in the tonsil, base of the tongue, or hypopharynx.

The histologic picture also may indicate the site of the primary tumor. Undifferentiated carcinomas of the transitional-cell type may originate in the nasopharynx, base of the tongue, or tonsillar region. Keratinizing squamous-cell carcinoma more commonly arises in the tonsillar region or base of the tongue. Metastatic undifferentiated tumor, with a marked desmoplastic or scirrhous reaction, may spread from an undetected primary carcinoma of the thyroid. It is unusual for a carotid-body tumor to give regional or distant metastases.

If the location and the histologic type of the metastases strongly suggest origin from a particular area, it is reasonable to treat the metastases and presumed primary site of the tumor by radiation therapy. A neck dissection in the absence of a demonstrable primary site must be regarded as symptomatic treatment, but it is nevertheless occasionally effective in controlling the disease.

• PROLONGED BLEEDING AND DENTAL EXTRACTION

Q. A 50 year old man with a history of benign hypertension has been receiving DICUMAROL® following myocardial infarction four months ago. He has frequent anginal episodes on even moderate activity. An electrocardiogram made on admission to the hospital showed only inverted T waves in all precordial leads. Tracings one week later were normal.

Dental evaluation reveals numerous abscesses and extensive odontoclasis. Since the patient began taking Dicumarol, he has had frequent, mild bleeding from the socket of a loose tooth. The dentist refuses to extract any teeth until the prothrombin time is normal.

What treatment would best prepare this patient for dental extraction? Should vitamin K or menadione be administered orally or parenterally? Would it be better to change the medication to heparin? If so, when should this change be made? Should the heparin be administered intravenously or intramuscularly? For how long should the anticoagulant be withheld? What anesthetic should be used?

M.D.—New York

A. Dental extraction or dental surgery is absolutely contraindicated in this patient until the prothrombin time is normal. The effect of Dicumarol can be overcome by discontinuing its use and administering 72 mg. HYKINONE® intravenously. This may be repeated if necessary. As soon as the prothrombin time is normal, the extractions may be done. When the oral surfaces are healed, administration of Dicumarol may be resumed if the attending physician feels it is indicated. There would be no reason to give heparin to this patient unless an emergency arises which indicates its use.

Patients with coronary disease have very little difficulty with anesthetics. The oral surgeon, after consulting with the attending physician concerning the patient's general condition, is best qualified to select the anesthetic.

What's happening in Medicine

POSTGRADUATE MEDICINE'S REPORT of late news of interest to practicing physicians

EARLY DETECTION OF SPONDYLOARTHRITIS

Canadian Association of Radiologists:

• Spondyloarthritis may be diagnosed roentgenographically within a week after the onset of symptoms. The first roentgenographic evidence is narrowing of the affected intervertebral disk, usually in the lumbar region.—Dr. Arthur E. Childe, Children's Hospital of Winnipeg, Winnipeg.

• Radiation therapy with cesium 137 permits use of a small head while achieving a depth dose similar to that of cobalt 60 at 15 to 35 cm. and to that of conventional x-ray units at 50 cm.—Dr. D. J. Wright, Toronto General Hospital, Toronto.

SAME VIRUS AFFECTS TWO SPECIES

150th Anniversary, Massachusetts General Hospital:

• The same virus has caused leukemia in two kinds of animals. Under certain conditions, the virus which produces lymphocytic leukemia in mice has produced myeloid leukemia in rats.—Dr. Ludwik Gross, Veterans Administration Hospital, New York.

CELL SENSITIVITY TO IONIZATION

Conference on Radiobiology:

• A study was conducted to determine the response of neoplastic cells in vitro to ionizing radiation. Various cell types in the outgrowth of the same tissue explant responded differently to an equal dose of radiation. When particles of embryonal kidney were irradiated and cultivated in vitro, the lymphocytes, leukocytes, macrophages and fibroblasts were selectively destroyed as radiation dosages were gradually increased, while the renal epithelial cells continued to proliferate. Mammary tumors of similar morphologic structure differed significantly in their response to equal doses. Recent studies of the radiosensitivity of tumor cells indicated that the quality and quantity of mitochondria may play a significant role in determining cellular radiosensitivity.—Dr. Anna Goldfeder, New York University School of Medicine, New York.

• Parts of single cells have been irradiated with alpha radiation by placing microneedles tipped with polonium near them. The well-defined range of the polonium alpha particles enables the radiation to be confined to a region at one end of the cell and permits part of the cytoplasm to be irradiated while the nuclear region remains untouched.—Dr. T. R. Munro, Strangeways Research Laboratory, Cambridge, England.

Hypothermia for gastric hemorrhage

Sectional meeting, American College of Surgeons:

• Gastric hypothermia has controlled massive hemorrhage of the upper part of the gastrointestinal tract in 85 per cent of a group of patients. The cooling is obtained with a balloon attached to a coaxial tube and passed into the stomach.—Dr. Stephen L. Wangensteen, Presbyterian Hospital, New York.

Placental insufficiency

Royal College of Physicians and Surgeons of Canada:

• A review of 40 cases of placental insufficiency showed that the high-risk pregnant woman is more than 30 years of age, has a history of previous abortion or delivery of an immature or premature infant, gains less than 15 lb., and has a fundic height less than that expected for the gestational age. Almost 40 per cent of the women in the cases reviewed produced stillborn infants, and 17 per cent produced live infants who were seriously affected by respiratory distress, intracranial hemorrhage and malnutrition.—Dr. W. Dennis Fraser, Royal Victoria Hospital, Montreal.

Progress report on synthetic penicillin

Western Association of Physicians:

• The semisynthetic compound dimethoxyphenylpenicillin continues to be free of resistant bacterial strains. Its continued effectiveness may be due to its own resistance to destruction by penicillinase. No unusual side effects have been seen.—Dr. William M. Kirby, University of Washington School of Medicine, Seattle.

Hearing loss after stapedectomy

Midwinter Convention in Ophthalmology and Otolaryngology:

• Two per cent of patients have a hearing loss after stapedectomy. This is believed to be caused by trauma resulting from the drilling required to remove extensive sclerotic deposits around the stapes.—Dr. Harold F. Schuknecht, Henry Ford Hospital, Detroit.

Estrogen aids heart victims

American Federation for Clinical Research, Western Section:

• PREMARIN®, a preparation of conjugated equine estrogens, improved the survival rate in a group of 62 men who had had one or more heart attacks, as compared with a control group. During a period of 3 to 18 months of uninterrupted treatment, only three of the 62 men died, whereas 17 of the 123 men in the control group died.—Dr. Jessie Marmorston, University of Southern California School of Medicine, Los Angeles.

Synthetic ACTH used in man

The Endocrine Society:

• A study of the action of synthetic ACTH in two young men showed that it stimulates human adrenal function, as indicated by the increased urinary excretion of the adrenal steroid fractions 17-ketosteroids, aldosterone and hydrocortisone. The synthetic ACTH contains 19 of the 39 amino acids found in natural corticotropin extracted from the pituitary glands of animals. Its potency is about two-thirds that of the pure, natural ACTH molecule. The findings indicate that a synthetic hormone might be useful in treating collagen diseases. Synthetic fractions might be made for specific purposes.—Dr. Peter H. Forsham, University of California School of Medicine, Berkeley-San Francisco.

Now...two new products to supply the iron they need at the ages they need it

TRI-VI-SOL®

VITAMIN DROPS WITH IRON

DECA-VI-SOL®

CHEWABLE VITAMINS WITH IRON

These two new formulations—one for infants, one for older children—are distinctive additions to the present line of Vi-Sol® vitamins, thereby providing the choice of Tri-Vi-Sol drops with and without iron and Deca-Vi-Sol chewable vitamins with and without iron. Both new products taste good. The packaging carefully limits elemental iron to a total of 500 mg. per bottle. Nevertheless, the bottles should be kept out of the reach of children.

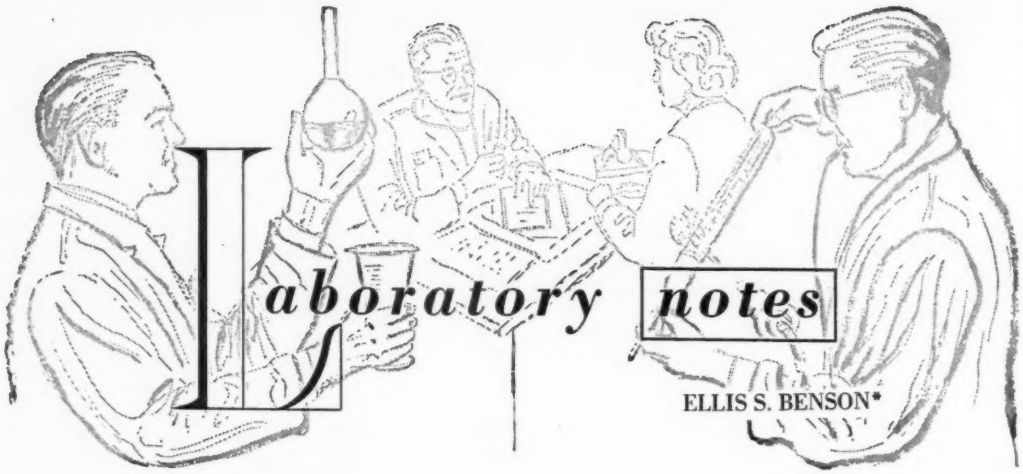
Tri-Vi-Sol vitamin drops with iron. **Each 0.6 cc. daily dose supplies 10 mg. elemental iron plus safe, rational amounts of vitamins C, D and A. Supplied in bottles of 30 cc.**

Deca-Vi-Sol chewable vitamins with iron. **Each chewable tablet supplies 10 mg. elemental iron and safe, rational amounts of C, D and A plus seven significant B vitamins. Supplied in bottles of 50 chewable tablets.**

10 mg. of prophylactic iron... logically combined for your convenience with two of the most widely used and accepted pediatric vitamin products

E7161

UNIVERSITY OF MICHIGAN LIBRARIES



Photometers: Selection, Use and Maintenance

MYRTON F. BEELER

Ochsner Foundation Hospital, New Orleans

In clinical chemistry, much depends on photometric methods of analysis. Photoelectric instruments are available which are reasonably priced, quite durable and dependable, easily used, and capable of yielding accurate results when properly used. Unfortunately, the very ease of operation may lead the unwary to uncritical misuse of these instruments. Instrument manufacturers all too often court such misuse by ignoring or understressing in instruction manuals the fallibilities of a particular instrument, and they bolster false confidence in the user by supplying photoelectric colorimeters precalibrated for a number of analytic procedures.

Dr. Beeler, director of clinical laboratories, Ochsner Foundation Hospital, New Orleans, discusses briefly in this month's column some of the pitfalls in the acquisition and use of photometers and describes measures by which these may be avoided.—Ellis S. Benson, M.D.

*Director of Hospital Laboratories and Associate Professor of Clinical Medicine and of Pathology, University of Minnesota Medical School, Minneapolis, Minnesota.

MYRTON F. BEELER

MANY analytic studies now performed in clinical laboratories are photometric; that is, monochromatic light transmitted by a substance in solution is measured by means of a photometer, and the concentration of the substance is subsequently calculated by comparison with the light transmitted by a standard solution. The accuracy and precision of these measurements depend in part on the photometer employed and on proper use and maintenance of the instrument.

A schematic diagram of a simple filter photometer is shown in figure 1; a spectrophotometer is diagramed schematically in fig-

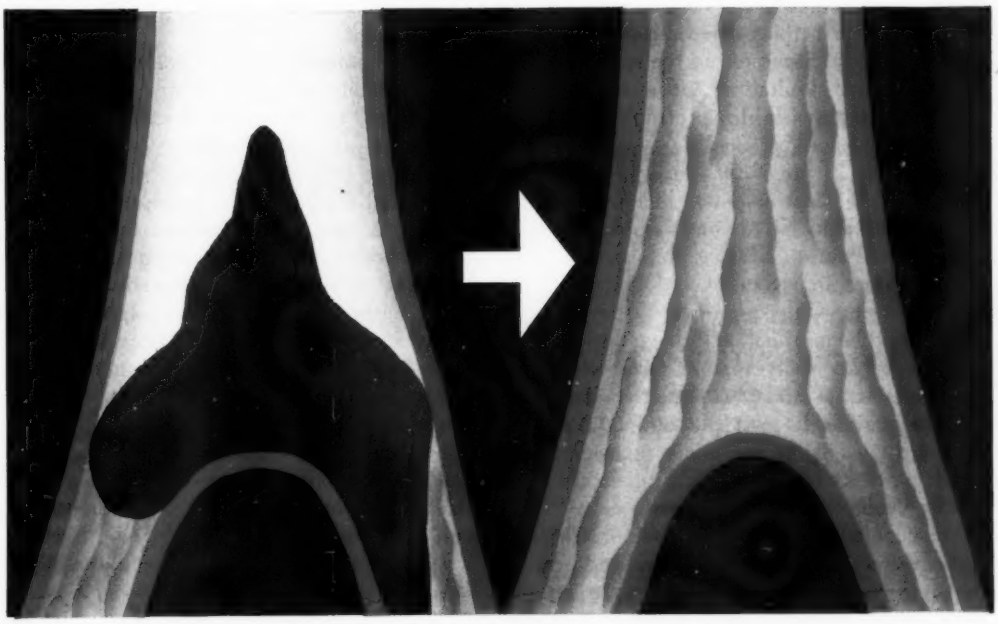
(Continued on page A-44)

clinical endorsement grows as proof accumulates

ACTASE
TRADEMARK

Fibrinolysin (Human)

NOT JUST A NEW DRUG... *A NEW THERAPY*



Ortho

SPECIFIC FOR THE DISSOLUTION
OF INTRAVASCULAR CLOTS

UNIVERSITY OF MICHIGAN LIBRARIES

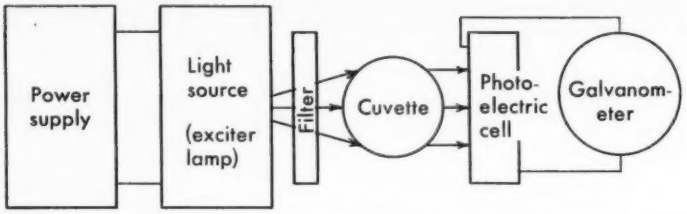


FIGURE 1. Schematic diagram of a filter photometer.

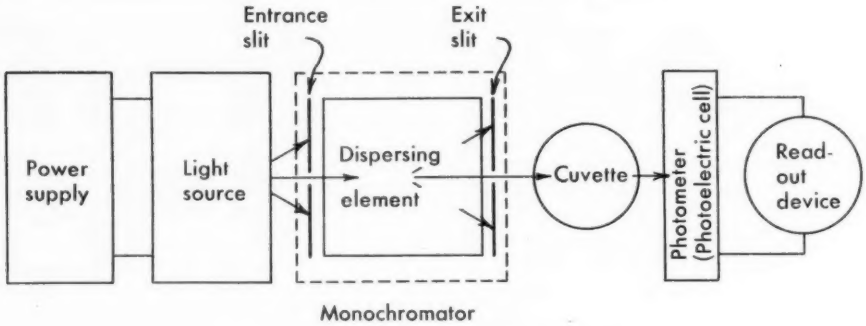


FIGURE 2. Schematic diagram of a spectrophotometer.

ure 2. An illuminating but concise description of the basic principles of spectrophotometry, together with a discussion of the special characteristics and limitations of a number of commercially available spectrophotometers, has recently been published.[1]

A number of points should be considered before such an instrument is purchased. The apparatus should be reasonably priced, ruggedly constructed, simple to operate, and capable of rapid, accurate and reproducible measurements. Galvanometer instability or drift should be minimal, and the galvanometer dial should be easily read. Exciter and galvanometer lamps and photosensitive elements (photoelectric cells and phototubes) should be readily accessible for quick replacements. Spare parts and expert servicing should be readily available without excessive cost.

The cuvette holder should be so constructed that cuvettes may be easily inserted and firmly held in proper, constant alignment. It should be possible to insert and remove cuvettes without scratching their surfaces. Accidental breakage of a cuvette or spillage of corrosive solutions should not readily result in serious damage to the instrument, and provision should be made for direct, rapid drainage in such a case.

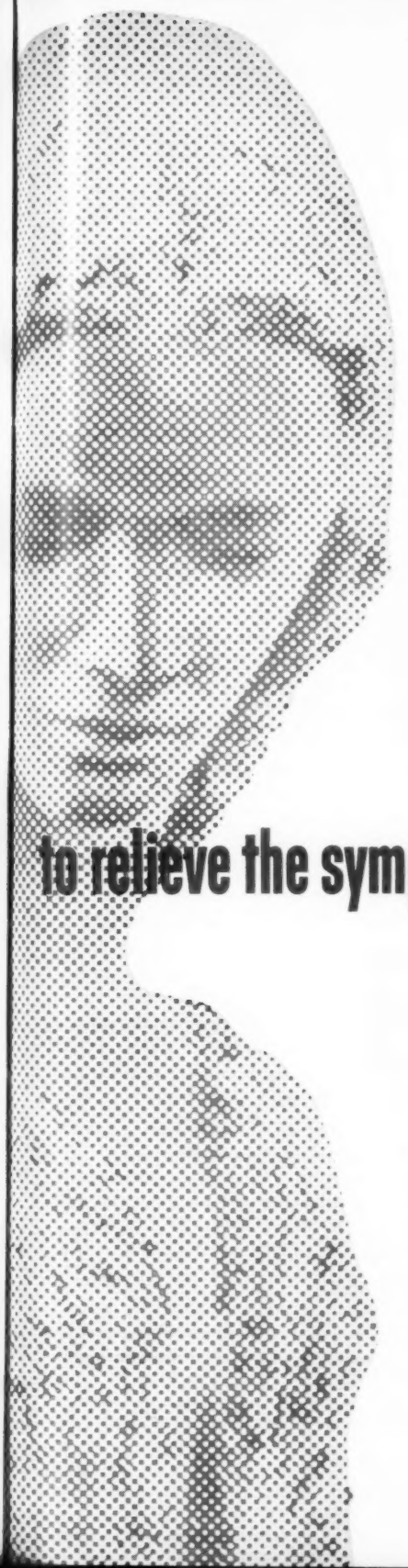
The photometer should operate with light of reasonably narrow bandpass. The term "bandpass" refers to the wavelength spectrum of a beam of light. By definition, monochromatic light is light of a narrow range of wavelength and thus of narrow bandpass.

With a spectrophotometer, the manufacturer should provide the means for rapid checking of wavelength calibration, and the wavelength should be easy to adjust. The instrument should be capable of providing linear graphs when absorbency is plotted against concentration, although this does not demonstrate linearity of photosensitive elements, as pointed out by Cannon and Butterworth.[2] One must rely on the manufacturer to provide linear components (figure 3) although he may not always do so.[3]

Finally, acceptance of the apparatus by the technical personnel regularly using it is important. Therefore, it is highly desirable that the distributor provide for a trial period of two weeks.

Once the photometer has been selected, its

(Continued on page A-46)



CYCLEX®

HYDRODIURIL® WITH MEPROBAMATE
HYDROCHLOROTHIAZIDE

to relieve the symptoms of premenstrual tension

for EDEMA ... **CYCLEX provides the prompt diuresis of HYDRODIURIL for rapid reduction of weight gain, breast fullness, abdominal congestion**

for MOOD-CHANGES ... **CYCLEX supplies the effective relief of meprobamate for nervousness, irritability, tension, nausea, malaise, insomnia**

for GI DISTRESS ... **CYCLEX affords quick-acting relief of nausea and bloating associated with premenstrual tension**

SUPPLIED: **Tablets, bottles of 100. Each tablet contains 25 mg. of HYDRODIURIL (hydrochlorothiazide) and 200 mg. of meprobamate.**

DOSAGE: **Usual adult dosage is one tablet once or twice a day, beginning on the first morning of symptoms and continuing until the onset of menses. CYCLEX may be continued through the menstrual period.**

Before prescribing or administering CYCLEX, the physician should consult detailed information on use accompanying package or available on request.

CYCLEX and HYDRODIURIL are trademarks of Merck & Co., Inc.

MSD

MERCK SHARP & DOHME
Division of Merck & Co., Inc.
West Point, Pa.

UNIVERSITY OF MICHIGAN LIBRARIES

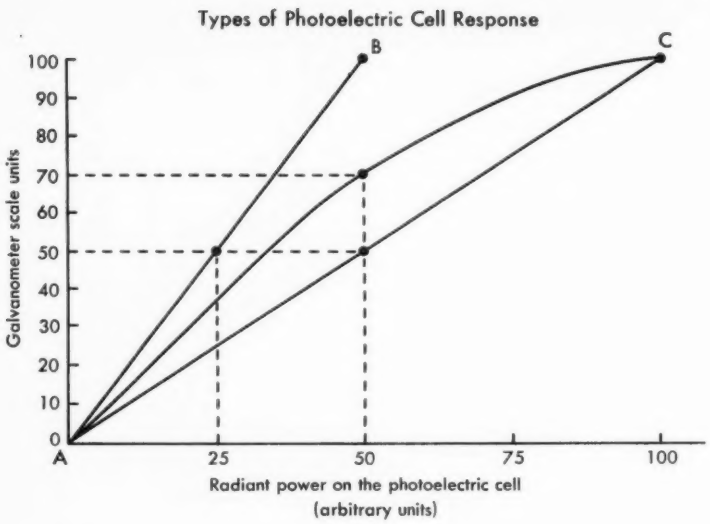


FIGURE 3. Galvanometer scale readings as related to radiant power of linear and nonlinear photoelectric cells. Lines AB and AC represent the response of two photoelectric cells of varying sensitivity to varying amounts of irradiance.

The response of these photoelectric cell galvanometers is linear and is contrasted with that of a photoelectric cell galvanometer represented by curved line AC, which shows a nonlinear response to irradiance.

use and maintenance deserve consideration. It should preferably be placed in a quiet area, away from excessive light and vibration. For example, it should not be placed directly under an overhead light or near a window through which sunlight may come. Neither should it be placed immediately adjacent to its transformer, since this may affect its electric stability.

The optical system should be kept free from scratches, finger marks, protein films and dirt. Cuvettes should be calibrated by the user. This may be done by reading the same solution of hemoglobin, potassium dichromate or alkaline ammoniated cupric sulfate in a number of cuvettes, selecting and marking for proper orientation those falling within the desired range. A line may be cut on the cuvette surface to correspond with a similar mark on the cuvette holder in the position in which the cuvette is to be read. A sufficient number of cuvettes must be available to permit cleaning and drying of each one before it is used again.

With spectrophotometers, calibration of the wavelength scale should be checked frequently, and appropriate adjustments should be made when indicated.

Potentiometer coils should be checked occasionally by slowly revolving their control knobs while observing the galvanometer for erratic movement. If defects are found, they may be corrected at times by rapidly reversed movements of the control knob over the defective area. If this is not effective, a small piece of nonconducting, fine abrasive paper may be fixed on the sweeping arm of some photometers, and the knob may be rotated back and forth a few times.

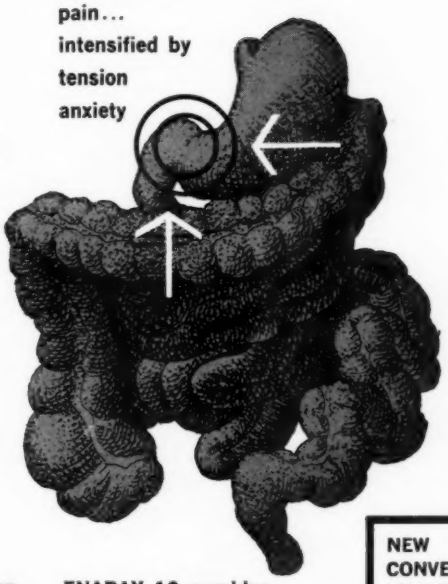
Whenever stable standards are available, several should be included in each set of determinations, and these should duplicate the range of values expected to be encountered with the unknown. Use of calibration curves or factors provided by the manufacturer is not an acceptable practice. Because stable standards are not available for all procedures, at times recourse must be made to calibration curves prepared by the person who uses the instrument, but these curves must be checked occasionally with standard solutions.

A simple daily check of the photometer should be performed to detect instrumental alterations which could lead to error. One such method[4] is to set the instrument to read 100 per cent transmission with distilled water; the cuvette is then removed and the galvanometer reading is recorded with no cuvette in place (air blank). This reading has been

(Continued on page A-48)

double trouble of the g.i. tract?

spasm
hyperacidity
pain...
intensified by
tension
anxiety



dual action in the therapeutic attack

ENARAX 10 provides
10 mg. oxyphencyclimine
the inherently
long-acting anticholinergic
plus 25 mg. ATARAX®†
the tranquilizer
that does not stimulate
gastric secretion

NEW
CONVENIENT
LOW DOSAGE
NOW AVAILABLE

ENARAX 5

Oxyphencyclimine HCl .....**5** mg.
ATARAX (Hydroxyzine HCl) ...25 mg.

1 tablet twice daily
Supplied: Bottles of 60
scored white tablets.

ENARAX®

A SENTRY FOR THE G.I. TRACT **B.I.D.**

Proven effective for continuous relief of both physical and emotional aspects of G.I. disease — hypermotility, hyperacidity, and hyperemotivity. One tablet b.i.d. provides 24-hour control of symptoms in peptic ulcer, gastritis, gastroenteritis, colitis, functional bowel syndrome, duodenitis, hiatus hernia (symptomatic), irritable bowel syndrome, pylorospasm, cardiospasm, biliary tract dysfunctions, and dysmenorrhea. ENARAX 10 has been successful in 92% of cases.[1-3] Let your G.I. patients profit from its dual, full-time therapeutic action.

Dosage: One ENARAX 10 tablet twice daily — preferably in the morning and before retiring. The maintenance dose should be adjusted according to the therapeutic response. Use with caution in patients with prostatic hypertrophy and only with ophthalmological supervision in glaucoma. **Supplied:** In bottles of 60 black-and-white scored tablets. Prescription only.

References: 1. Hock, C. W.: Am. J. Gastroenterol. **34**:293 (Sept.) 1960. 2. Leming, B. H., Jr.: Clin. Med. **6**:423 (Mar.) 1959. 3. Data in Roerig Medical Department files.

†brand of hydroxyzine

FOR HEMATOPOIETIC STIMULATION WHERE OCCULT BLEEDING IS PRESENT **HEPTUNA® PLUS** THE **COMPLETE** ANEMIA THERAPY

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being®

UNIVERSITY OF MICHIGAN LIBRARIES

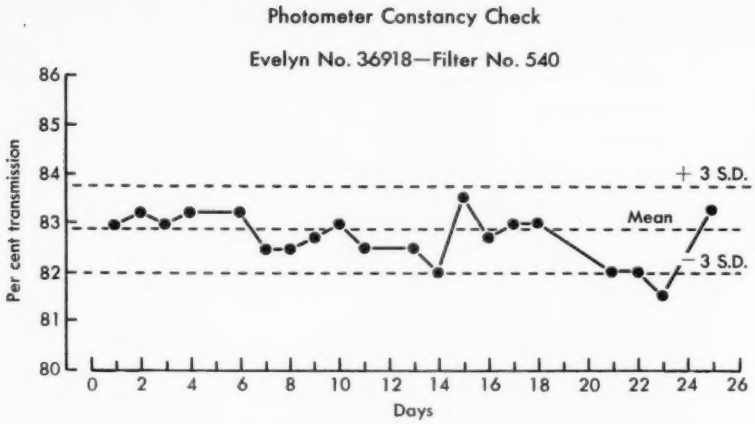


FIGURE 4. Graph of daily readings obtained on an Evelyn photometer during constancy checking of the instrument, as described in the text.

(Figures 3 and 4 are reprinted from Beeler.[4])

termed the "center setting." If the galvanometer reading drifts off scale when this is done, the procedure may be varied so that the galvanometer is set at 100 per cent transmission with no cuvette in place (air blank). The cuvette containing distilled water is then inserted into the holder and the galvanometer reading is recorded. (It will be on scale.) Readings of this type may be made daily and recorded. Daily results should be reasonably reproducible (figure 4). A consistent trend toward higher readings or significant loss of reproducibility may be due to loss of photoelectric cell linearity or sensitivity or to some change in the alignment of the optical system. The latter may result from change in the exciter lamp bulb, dirty or scratched cuvettes, or accidental exchange of filters. The last-mentioned situation may cause a change in reading even when the filter is ostensibly of the same wavelength range as the one used in the series of calibration readings.

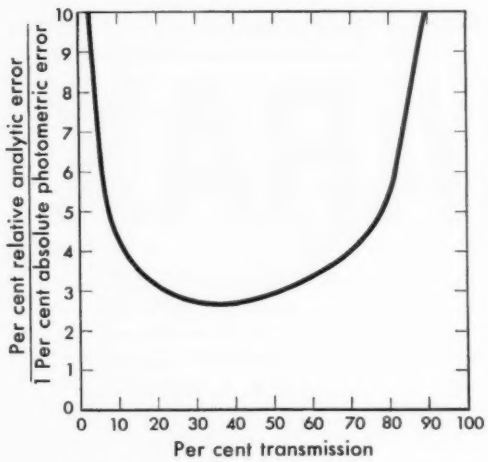


FIGURE 5. Relative analytic error for an absolute photometric error of 1 per cent as a function of the percentage light transmission.

(From Glick, Engstrom and Malmstrom.[6])

With a new instrument, readings of the type just described should be made hourly for a day or two as a check on the constancy of the voltage source.

For reasons having to do with application of Beer's law, use of the scale of transmission readings should be restricted, when possible, to the region between 10 and 80 per cent transmission.[5,6] The relative analytic error is high below 10 per cent and above 80 per cent transmission, as illustrated by figure 5. Filters should be selected and concentrations of standards and determinants should be adjusted so that readings fall within the 10 to 80 per cent range of light transmission.

The development of photometers during this century has made possible widespread, effective use of a variety of photometric analytic studies in clinical laboratories. The instruments vary in cost, reliability, operating simplicity and ease of maintenance. The valid-

(Continued on page A-50)

IN BRIEF

TYZINE is tetrahydrozoline hydrochloride, a sympathomimetic amine with potent decongestant properties. Relief is almost immediate and lasts four to six hours after a single administration. Virtually free of sting or burn and rebound congestion . . . odorless and tasteless. TYZINE is not significantly absorbed systemically when used as directed . . . does not impair ciliary activity . . . and is physiologically buffered to pH 5.5.

INDICATIONS: Relieves inflammatory hyperemia and edema of the nasal mucosa and congestive obstruction of sinus and eustachian ostia, as may occur in the common cold, hay fever, perennial vasomotor rhinitis, chronic hypertrophic rhinitis, and sinusitis.

DOSAGE AND ADMINISTRATION: Adults and Children 6 Years and Over—2 to 4 drops of TYZINE (0.1%) in each nostril as needed, not more often than every three hours. When using TYZINE Nasal Spray, insert tip of plastic bottle into nostril, tilt the head slightly forward from an upright position, and squeeze sharply 3 or 4 times, not more often than every three hours.

Important: Use TYZINE Pediatric Nasal Drops (0.05%) for children under 6 years. The 0.1% concentration is contraindicated in this age group.

SIDE EFFECTS: Transient mild local irritation after instillation has been reported in rare instances.

PRECAUTIONS: Avoid doses greater or more frequent than those recommended above. Use with caution in hypertensive and hyperthyroid patients.

Overdosage may cause drowsiness, deep sleep, and, rarely, marked hypotension in infants and young children. KEEP OUT OF HANDS OF CHILDREN OF ALL AGES.

SUPPLIED: *Nasal Solution*, 1-oz. dropper bottles, 0.1%. *Nasal Spray*, 15 cc., in plastic bottles, 0.1%. *Pediatric Nasal Drops*, ½-oz. bottles, 0.05%, with *calibrated* dropper.

More detailed professional information available on request.

Science for the world's well-being™ Pfizer PFIZER LABORATORIES *Division, Chas. Pfizer & Co., Inc. Brooklyn 6, New York*

UNIVERSITY OF MICHIGAN LIBRARIES

Your copies of

Postgraduate Medicine

are valuable

KEEP THEM FOR READY REFERENCE . . .

Custom-made for POSTGRADUATE MEDICINE, these binders will keep your copies clean, orderly and readily accessible for reference. Rich appearance of dark blue simulated leather cover and gold leaf embossed lettering make these binders a distinctive companion for your finest bindings. Gold foil provided for writing in volume number and year. Binders sent postpaid, carefully packed; 2 for $5.00, 4 for $9.50.

- Keeps current issues protected yet readily accessible
- Sturdy and attractive for your desk or library shelf
- Each binder holds one volume, 6 issues of POSTGRADUATE MEDICINE

ORDER FORM

POSTGRADUATE MEDICINE
Essex Bldg., Minneapolis 3, Minn.

2 Volume Binders $5.00 4 Volume Binders $9.50

Enclosed is $_____ for _____ binders to be sent postpaid

Name_____

Address_____

City_____ Zone____ State_____

ity of results obtained with them will depend in part on these factors.

It should be emphasized again that the use of precalibrated charts supplied by the manufacturer is not satisfactory practice. Use of these charts leads to unsuspected errors. Calibrations made by the person using the instrument under his particular set of operating circumstances is the only rational method of operation.

REFERENCES

1. LEWIN, S. U.: Spectrophotometers. J. Chem. Educ. 37:A401; A455; A507; A637 (July; August; September; October) 1960.
2. CANNON, C. G. and BUTTERWORTH, L. S. C.: Beer's law and spectrophotometer linearity. Ann. Chem. 25:168-170, 1953.
3. KANNER, O.: Measurement errors in clinical spectrophotometry. Am. J. Clin. Path. 29:310-318, 1958.
4. BEELER, M. F.: Behavior of photocells. Am. J. Clin. Path. 32:140-144, 1959.
5. KOLTHOFF, I. M. and SANDELL, E. B.: Textbook of Quantitative Inorganic Analysis. New York, The Macmillan Company, 1952, pp. 631-632.
6. GLICK, D., ENGSTROM, A. and MALMSTROM, B. G.: A critical evaluation of quantitative histo- and cytochemical microscopic techniques. Science 114:253, 1951.

3-way support for the aging patient...

ASSISTS PROTEIN UPTAKE
IMPROVES MENTAL OUTLOOK
AIDS NUTRITIONAL INTAKE

NEW

1 small capsule every morning

GEVRESTIN®

Geriatric Vitamins-Minerals-Hormones-d-Amphetamine Lederle

Each capsule contains: Ethinyl Estradiol 0.01 mg. • Methyl Testosterone 2.5 mg. • d-Amphetamine Sulfate 2.5 mg. • Vitamin A (Acetate) 5,000 U.S.P. Units • Vitamin D 500 U.S.P. Units • Vitamin B_{12} with AUTRINIC® Intrinsic Factor Concentrate 1/15 U.S.P. Unit (Oral) • Thiamine Mononitrate (B_1) 5 mg. • Riboflavin (B_2) 5 mg. • Niacinamide 15 mg. • Pyridoxine HCl (B_6) 0.5 mg. • Calcium Pantothenate 5 mg. • Choline Bitartrate 25 mg. • Inositol 25 mg. • Ascorbic Acid (C) as Calcium Ascorbate 50 mg. • l-Lysine Monohydrochloride 25 mg. • Vitamin E (Tocopherol Acid Succinate) 10 Int. Units • Rutin 12.5 mg. • Ferrous Fumarate (Elemental Iron, 10 mg.) 30.4 mg. • Iodine (as KI) 0.1 mg. • Calcium (as $CaHPO_3$) 35 mg. • Phosphorus (as $CaHPO_4$) 27 mg. • Fluorine (as CaF_2) 0.1 mg. • Copper (as CuO) 1 mg. • Potassium (as K_2SO_4) 5 mg. • Manganese (as MnO_2) 1 mg. • Zinc (as ZnO) 0.5 mg. • Magnesium (MgO) 1 mg. • Boron (as $Na_2B_4O_7.10H_2O$) 0.1 mg. Bottles of 100, 1000.

LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

pproach to birth control

emko®
VAGINAL FOAM*

sing principles never before applied to contraceptives

• THE FIRST AEROSOL FOAM!

The volume of the material is expanded ten times to create A BLOCK OF FOAM.

• THIS BLOCK SEALS THE CERVICAL OS.

Only a FOAM can successfully serve this diaphragm-like function . . . without interfering with normal intercourse or reducing sensory contact.

• A HIGHLY EFFECTIVE PROVEN SPERMICIDE

EMKO Vaginal Foam contains the widely used and thoroughly proven spermicide Nonyl phenoxy polyoxyethylene enthanol 8.0% and Benzethonium Chloride 0.2%.

The total surface area of each bubble of foam contains this highly effective spermicidal combination. As the sperm attempts to penetrate the block of foam, its zig-zag course exposes it constantly to this very large contact area created by the bubbles.

Thus, Emko Vaginal Foam assures maximum spermicidal exposure . . . with a minimum weight of material.

• No douching . . . it vanishes after use **• Absolutely no greasiness or "after-mess"**
• No diaphragm . . . the foam does the blocking **• No irritation for husband or wife**

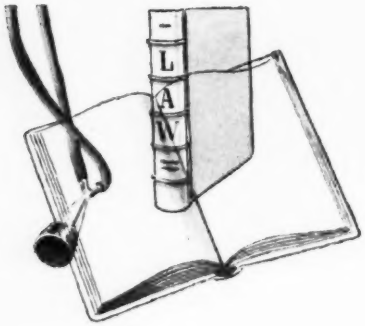
MARGARET SANGER RESEARCH BUREAU/**INTERIM REPORT**

In the Contraception Service of the Margaret Sanger Research Bureau, through October 31, 1960, Emko had been used from one to 22 months by 362 patients, with a total of 12 unplanned pregnancies. Seven of the pregnant patients admitted irregularity in the use of Emko.

Two planned pregnancies had also occurred after stopping the use of Emko.

A. J. SOBRERO, M.D. *Research Director*

*PAT. NO. 2,943,979, OTHER PATS. PEND.



Forensic Medicine

A Law-Medicine Forum: Personality Disorders

OLIVER C. SCHROEDER, JR.,* MORRIS M. KESSLER† AND EDWARD J. SCHIFF‡

Cleveland

THE current basic challenge in the medico-legal area is to provide medical knowledge for legal solutions to human conflicts. This challenge is not easy to meet when the human conflict revolves around the medical frontier of personality disorders. To indicate the ramifications of the challenge, Drs. Kessler and Schiff provide observations on a case history involving a personality disorder with legal implications.

Case Report

A 23 year old man received an injury in an automobile accident which resulted in total blindness in one eye and a cosmetic defect to the face. After the accident he did not work for two years. Since then he has worked only in a minor capacity. He is pessimistic concerning the surgeon's possible success in correcting the cosmetic defect. His good eye fatigues easily, causing him to worry about driving. He can read only about 10 minutes at a time.

Prior to the accident, this young man was fairly well adjusted; he was a good athlete, played varsity basketball, and dated girls. Since the accident he has participated in some sports but is restricted in his activity. He goes out stag; although he dances with girls, he has not dated for nine months. He is sensitive about going to new places, and is self-conscious about the injury. He rationalizes that his desire for girls' company will return. He believes that God is punishing him for evil-doing. He feels he has musical talent but is apathetic about pursuing it.

Legal analysis—The accident, which blinded this young man in one eye, caused a cosmetic defect, and affected his personality, creates basic legal problems. In Biblical times the law placed liability for such injury on the person inflicting the injury ("an eye for an eye"). In the Middle Ages the law refined the relationship and required existence of not only a causal relationship but also a particular mental attitude by the doer of the injurious act (intent to injure or negligence which caused injury). Today the lawyer seeking compensation for his client must prove (1) the fault of the person inflicting the injury, who is called a tort-feasor or a wrongdoer, and

(Continued on page A-62)

*Director, Law-Medicine Center and Professor of Law, Western Reserve University, and POSTGRADUATE MEDICINE's Editor for Forensic Medicine; †Clinical Psychiatrist, Cleveland; ‡Senior Instructor in Child Psychiatry, Western Reserve University, Cleveland, Ohio.

Vertigo is reversible

Antivert® STOPS VERTIGO

moderate to complete relief of symptoms in 9 out of 10 patients'

Prescribe one ANTIVERT tablet (or 1-2 teaspoonfuls ANTIVERT syrup) 3 times daily, before each meal, for prompt relief of vertigo, Meniere's syndrome and allied disorders. Side effects are short-lived, usually only harmless flushing and tingling associated with vasodilation. ANTIVERT is contraindicated in severe hypotension and hemorrhage.

Supplied: Small blue-and-white scored tablets (meclizine HCl 12.5 mg. and nicotinic acid 50 mg.) in bottles of 100. Syrup in pint bottles. Prescription only. Bibliography available on request.

And for your aging patients—
NEOBON® Capsules: five-factor geriatric supplement.

Reference: 1. Scal, J. C.: Eye Ear Nose & Throat Month. 38:738 (Sept.) 1959.

ROERIG

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being®

now available: *Antivert* **syrup**

Each teaspoonful (5 cc.) contains 6.25 mg. meclizine HCl and 25 mg. nicotinic acid.

SHERROD LIBRARY OF MEDICINE UNIVERSITY

(2) injury directly caused by the act of the tort-feasor.

In the present case, we have assumed that the young man was injured by a tort-feasor. His blindness and cosmetic defect were direct results of the accident. The truly challenging legal issues, however, are (1) whether the personality disorders can be directly charged to the accident, and (2) whether these disorders are permanent. The extent of this man's injuries and the evaluation of the disabilities create major legal problems which demand solution through medical facts and opinions.

Medical discussion—DR. KESSLER: One approach is to note that the injury has caused a defect in both function and appearance. The effect has been some withdrawal, perhaps an early stage. Thus, we need to know what type of personality is involved. The injury has occurred to a personality at a particular level. What has this new stress done to that particular personality? What type of person was this young man before the injury?

The history indicates he was quite outgoing and interested in physical activities, as evidenced by his being an athlete. That type of person attaches particular importance to each part of the body, and this young man has an exalted body image. The injury to the eye then goes to the very heart of the personality; it is painful for him to adjust to the injury, and he gradually builds up defenses. The study of the defenses gives an idea of the neurotic effect of the physical injury on the personality.

In studying the mind, we find that its whole energy system is directed both inward and outward. As we grow older this energy is released to objects outside ourselves. This affects various organs of the body; each part has a particular charge to it. When one part is injured there is a reshuffling of this energy; it is withdrawn from other organs and localized in the injured part in an effort to heal and defend that part.

With a direct injury, a constant sensation comes to the injured part from the nervous system, and this must be handled. One of the things that can happen is a withdrawal of energy directed toward objects in the outer world (sports, girls, a career) and the transferal of this energy back into the self. You see in it a protective state, in the attempt to heal and to re-establish balance; however, it is a pathologic rather than a normal pattern.

The effects of an injury are frequently like those of this young man, i.e., withdrawal and increasing concern about oneself. There is a regression in which old problems reappear. Frequently, when young people start thinking about punishment by God, their sexual anxieties become aroused. Although this may not be a fully conscious reaction, it is related to the idea of chastisement. What did I do wrong to receive this punishment? This begins to ferment and creates a pathologic mental condition, so that in addition to the physical injury there is an effect on the personality. You have to consider both, and in this situation it is probably compensatory.

DR. SCHIFF: As far as medical facts go, I would want to know how this injury occurred, i.e., under what circumstances the patient was injured. What kind of work was he doing? Did any carelessness on his part cause the injury? If so, perhaps this patient had some need to have the injury. This is speculation, but one of the things we would want to know.

Other medical facts we would want to know are whether the injured eye was replaced by an artificial one and how well the good eye functions. What has the patient's doctor advised about his driving? Has the patient withdrawn so that his inability to drive is not physical but psychologic, based on a fear that something might happen to his remaining eye? How long was he in the hospital? Did he have an acute anxiety attack due to covering of the good eye in the hospital? Some people experience great anxiety in such circumstances when the good eye is deprived of vision by covering, although it may be a necessary medical procedure.

It also would be important to know how this man reacted to any injury in the past. Has he been preconditioned to an injury? Has he previously reacted by withdrawal? Is he accident-prone? The effect of his cosmetic defect on people around him should be ascertained. How did his family handle the situa-

(Continued on page A-64)

the choice--by acclamation!
for ringworm therapy

Schering

In the less than 2 years since griseofulvin—first orally effective antifungal antibiotic—was introduced, over 250 leading investigators have published over 150 clinical reports and reviews in 20 countries concerning results in over 4,500 patients with dermatomycoses. Almost all of the patients benefited from griseofulvin.

S-727

oral

fulvicin

22:10. 1959. (2) Andrews, G. C.; Domonkos, A. N., and Silva, A., Jr.: J.A.M.A. 173:1542, 1960. (3) Arnold, H. L., Jr.: Straub Clin. Proc. 25:53, 1959. eaves, C. K., and LaTouche, C. J.: Brit. M. J. 2:1141, 1959. (5) Barnett, S. M.: Wisconsin M. J. 59:421, 1960. (6) Baruffini, A.: Farmaco (Ed. Sc.) 14: U. S. Armed Forces M. J. 11:1001, 1960. (8) Beare, M., and Mackenzie, D.: Brit. M. J. 2:1137, 1959. (9) Behrman, H. T.; Lubowe, I. I.; Mandel, E. 59-1960. (10) Belisario, F. C., and Havyatt, M. T.: Dermatologica 119:158, 1959. (11) Bensel, A.; Am. J. Dis. Child. 100:131, 1960. (12) Berry, C. Z ch. Dermat. 81:982, 1960. (13) Birt, A. R.; Hoogstraten, J., and Norris, M.: Canad. M.A.J. 81:165, 1959. (14) Blank, H., and Roth, F. J., Jr.: A.M.A. A mith, J. G., Jr.; Roth, F. J., Jr., and Zajas, N.: J.A.M.A. 171:2168, 1959. (16) Blank, H., and Smith, J. G., Jr.: A.M.A. Arch. Dermat. 81:779, 1960. (17) B (18) Borrie, P.: Practitioner 183:419, 1959. (19) Burgoon, C. F., Jr., et al.: A.M.A. Arch. Dermat. 81:724, 1960. (20) Cadbury, J. B.: St. Louis County L., et al.: North Carolina M. J. 21:109, 1960. (22) Cameron, O. J.: Nebraska M. J. 45:67, 1960. (23) Carney, R. G., and Ziebell, W. C.: J. Iowa M e, L. C.; Pelbois, O. F., and Rollier, R.: Maroc M. 39:74, 1960. (25) Chivington, P. V.; Gray, H. R.; Wolf, R. L., and Dalton, J. E.: J. Indiana Tullett, A.: Brit. M. J. 2:286, 1959. (27) Degos, R.: A.M.A. Arch. Dermat. 81:806, 1960. (28) Degos, R.; Rivallier, E., and Lefort, P.: Presse méd. 67:1 at. 81:849, 1960. (30) Desai, S. C.: Indian J. Dermat. & Venereol. 25:93, 1959. (31) Die Redaksie, V.: South African M. J. 33:433, 1959. (32) Dillah gt. 81:790, 1960. (33) Do [illegible] G.: New England J. Med. 260:1271, 1959. (34) Esteves, J., and Neves, H.: Dermatologica 119:125, 1959. (35) Evere l, 52:793, 1959. (36) F [illegible] Am. Podiat. A. 50:292, 1960. (37) Fergusson, [illegible] G.; Logan, J. C. P., and Derblay, P. R.: Brit. M. J. 1:1026, 1960 3:429, 1959. (39) F [illegible] E., and Supliki, D.: J. M. Soc. New Jersey 57:489, 1960. (40) Flint, A.; Forsey, R. R., and Usher, B.: Canad M. Women's A. 15 [illegible] (42) Flood, J. M.: Clin. Med. 6:2 [illegible] 95, 943. Flood, J. M., and Strehler, D. A.: Guthrie Clin. Bull. 28:72, 1959. (44 k, L.; Stetner, K.; K [illegible] and Chiaramonte, J.: New Yo [illegible] 60:23 [illegible] 1960. (46) Frey, J. R., and Gelick, H.: Dermatologica 119:132, 195 ovitch, T. A.: A.M.A. [illegible] Dermat. 82:415, 1960. (48) Gaethe, G.: J. Louisiana M. S. 111:302, 1959. (49) Gant, J. Q., Jr.; Gould, A. H., and Weiner, M. las, Texas, Dec. 1 [illegible] 59. (50) Goldberg, H. C.: J. Am. Podiat. A. 50:290, 1960. (51) Goldblatt, S.: J.A.M.A. 172:1643, 1960. (52) Goldfarb, N. J., Goldfarb, N. J., an [illegible] enthal, S. A.: Current M. Digest 26:67, 1959. (54) Goldfarb, N. J., and Sulzberger, M. B.: A.M.A. Arch. Dermat. 81:859, 19 38, 1959. (56) Gold [illegible] L., et al.: J.A.M.A. 172:532 [illegible] 0. (57) Goldman, L.; Preston, R. H., and Schwarz, J.: Acta Dermatovener. 39:454, 1959. (58 M.: A.M.A. Arch. D [illegible] 81:833, 1960. (59) Götz, [illegible] Med. Klin. 54:2162, 19 [illegible] (60) Gould, A. H.: M. [illegible] District of Columbia 29:72, 1960. (G 28:476, 1959. (62) [illegible] on, L. D., and Shair, H. M [illegible] n. Pharmacol. & Th [illegible] :624, 1960. (63) Gre [illegible] A.; Moss, E. L., Jr., and Foley, E. J.: E. F.; Bocobo, F. C [illegible] ery, F., and Miedler, L.: A [illegible] Arch. Dermat. 81:797, [illegible] 0. (65) Harvey, G.; Ale [illegible] er, J. O'D., and Kirk, J. F.: Scot. M. J. Wchnschr. 102:653, [illegible] (67 [illegible] H. J [illegible] Jank [illegible] De [illegible] e med. [illegible] 84:220 [illegible] 1959. (68) [illegible] on, K [illegible] R) 1171, 1960. (esk. 104:762, 1960 [illegible] John [illegible] S.: [illegible] nsin [illegible] 58 [illegible] 1959. (71) [illegible] son, [illegible] and [illegible] me [illegible] G. H.: [illegible] Biot, [illegible] 7:687, 1959-196 81:838, 1960. (73) K [illegible] ellen [illegible] , I., a [illegible] andbu [illegible] M.: H [illegible] ah 5 [illegible] :60, 1 [illegible] (74 [illegible] rman [illegible] H. Med [illegible] 55, 1 [illegible] (75) Khalafat, A.: d Aiello, L.: A.M.A. [illegible] Derm [illegible] 0:259 [illegible] 9. (7 [illegible] rk, J., [illegible] Mi [illegible] s, V. [illegible] M.A [illegible] n, Dermat. 8 [illegible] , 1960 [illegible]) Lata [illegible] : A.M.A. Arch. attner, H.: A.M.A. A [illegible] Derm [illegible] :863, [illegible] 0. (80 [illegible] n, H [illegible] en, H [illegible] nd [illegible] L.: A.M.A. A [illegible] Derm [illegible] :827 [illegible]) (81) Livingood 1960. (82) Loewenth [illegible] J. A.: [illegible] oc. [illegible] Africa [illegible] 3, 1959 [illegible] Lubowe [illegible] Cur [illegible] Podiat [illegible] 8:18 [illegible] 9. (84 [illegible] owe, [illegible] Antibiotic Med. and Nelson, W. O.: Proc. Soc. [illegible] Biol. & Med. [illegible] 59, 19 [illegible] (86) M [illegible] , and [illegible] , W. [illegible] Arch. Dermat. 81:758, 1960. (87 A. Arch. Dermat. 81:733, 1960. (88) Martin, A. R.: J. Invest. Dermat. 32:525, 1959. (89) Mathews, N.: J. Am. Podiat. A. 50:303, 1960. (90) M nzalez, B. B.: J.A.M.A. 171:2174, 1959. (91) McCuistion, C. H.; Lawlis, M. G., and Gonzalez, B. B.: A.M.A. Arch. Dermat. 81:761, 1960. (92) McDanie (93) Meara, R. H.: Brit. J. Dermat. 72:169, 1960. (94) Meenan, F. O. C.: Brit. M. J. 2:1485, 1959. (95) Meenan, F. O. C., and O'Connell, L. G.: Irish Indiana M. A. 52:1784, 1959. (97) Michalowski, B., and Gutaker, M.: Przegl. dermat. 47:111, 1960. (98) Midana, A., and Zina, G.: Minerva sconsin M. J. 59:425, 1960. (100) Morgan, H. G.: Western Med. 1:25, 1960. (101) Mullins, J. F.; Jampolsky, N. A., and Pinkerton, M. E.: llinois M. J. 117:121, 1960. (103) Newcomer, V. D., et al.: A.M.A. J. Dis. Child. 99:585, 1960. (104) Nierman, M. M.; Cohen, D. M., and Golden, M.: Illi and Pilot, J.: J. Indiana M. A. 52:1771, 1959. (106) O'Farrell, N. M.: A.M.A. Arch. Dermat. 82:424, 1960. (107) Pardo-Castello, V.: A.M.A. Arch. V.; Trespalacios, F.; Farinas, P., and Fernandez Baquero, G.: Bol. Soc. cubana dermat. sif. 16:1, 1959. (109) Peter, H.: Wien. klin. Wc G.: Brit. M. J. 1:1623, 1959. (111) Pettit, J. H. S.: Brit. J. Dermat. 72:158, 1960. (112) Pipkin, J. L.: A.M.A. Arch. Dermat. 81:813, 1960. (113) Praza Neil, B. S.: A.M.A. Arch. Dermat. 81:821, 1960. (114) Quero, R.: J. Invest. Dermat. 34:283, 1960. (115) Rees, R. B.; Bennett, J. H., and Greenlee, ss, F.: M. Circle Bull. 6:9, 1959. (117) Reiss, F.; Kornblee, L.; Gordon, B., and Villafane, J.: J. Invest. Dermat. 34:263, 1960. (118) Riehl, G.: H K., and Lofferer, O.: Dermat. Wchnschr. 141:161, 1960. (120) Rinaldi, V. G.: Minerva dermat. 35:77, 1960. (121) Robinson, H. M., Sr.: Bull. Schoo inson, H. M., Jr., et al.: A.M.A. Arch. Dermat. 81:66, 1960. (123) Robinson, H. M., Jr., and Robinson, R. C. V.: New Physician 9:3[illegible], 1960. (124) Rob (125) Robinson, H. C. V., and Robinson, H. M., Jr.: M. Times 88:66, 1960. (126) Rosenthal, S. A.; Goldfarb, N., and Baer, R. L.: J. Invest. Med. Canada 15:53, 1960. (128) Roth, F. J., Jr.; Sallman, B., and Blank, H.: J. Invest. Dermat. 33:403, 1959. (129) Russell, B., et al.: Lancet 1:1141, Axelrad, B.: J. Invest. Dermat. 33:85, 1959. (131) Sams, W. M.: A.M.A. Arch. Dermat. 81:802, 1960. (132) Sauer, G. C.: J. Kansas M. Soc. 61:279, 1960. Invest. Dermat. 34:295, 1960. (134) Sharpe, H. M., and Tomich, E. G.: Toxicol. & Appl. Pharmacol. 2:44, 1960. (135) Sidi, E., and Spinasse, J. B. Connecticut Med. 24:360, 1960. (137) Smith, N. G.: A.M.A. Arch. Dermat. 81:981, 1960. (138) Sternberg, T. H., et al.: Current Therap. Res. 1:1, 195 , and Maddin, S. W.: Canad. M.A.J. 81:726, 1959. (140) Sulzberger, M. B., and Baer, R. L.: Excerpta Med., Sect. XIII, Dermat. & Venereol. 13:145, 19 m. Osteopath. A. 59:370, 1960. (142) Vanbruseghem, R.: Bruxelles-m. 40:297, 1960. (143) Walker, M. H.: J. Am. Podiat. A. 50:297, 1960. (144) Weiner Columbia 28:423, 1959. (145) Welsh, A. L., and Ede, M.: Ohio M. J. 56:339, 1960. (146) Williams, D. I.: Brit. M. J. 2:1329, 1959. (147) Williams, D. I. Williams, D. I.: Practitioner 184:383, 1960. (149) Williams, D. I.; Marten, R. H., and Sarkany, I.: Lancet 2:1212, 1958. (150) Wilson, J. W.: M. Clin. North Pract. 23:14, 1960. (152) Wrong, N. M.: Canad. M.A.J. 80:656, 1959. (153) Wrong, N. M., and Rogers, S.: A.M.A. Arch. Dermat. 81:776, 1960. (154) Wr gers, S.: Canad. M.A.J. 81:167, 1959. (155) Yontef, R.: J. M. Soc. New Jersey 56:738, 1959. (156) Zinzius, J.: Deutsches med. J. 11:121, 1960.

tion? Did they overprotect him and thus contribute to his withdrawal? Are there any secondary so-called gains from not going back to preaccident activity?

I think in this situation psychologic tests would be of greatest value to help in a structured way to understand the symbolic significance of the cosmetic and eye defects. In such cases, psychologic tests elucidate factors which can be clinically determined only after long periods of talking with the patient. Not having extended time, we would use the tests. Even with sufficient time there are certain situations in which psychologic tests are of value; this is such a case. The testing would help us to understand certain unrecognized factors in the injury or in the reaction to it.

QUESTION: Do you feel that it is psychiatrically important that plastic surgery be performed on this man to cure the cosmetic defect? From the history he does not seem to have much hope that the surgeons can cure that defect.

DR. SCHIFF: This would depend on his surgeon's report. It is possible that the defect cannot be corrected. Certainly, if the medical reports show something could be done, it should be. However, it is important, even if some plastic repairs can be done, that this man not be rushed into surgery until his attitude toward the situation is determined. The surgery could possibly represent new trauma to him and give him more reason to worry.

QUESTION: Would you diagnose this case as a neurosis caused by the injury, that is, with a direct causal relationship?

DR. KESSLER: Yes. It triggered off latent things in the young man's personality. There is a very direct relationship between the injury and the precipitation of this neurosis, although you also must consider predisposing factors in his history that could flare up any time as neurosis.

QUESTION: What would be your prognosis?

DR. KESSLER: The prognosis would depend almost entirely on whether or not he has treatment. With treatment, he might be brought close to his previous state. You would have to work out the meaning of the injury to the point where he could adjust back to life again.

QUESTION: How long would treatment take?

DR. KESSLER: Intensive psychoanalytic treatment for an average person would require an hour a day, five days a week, for upward of two years. It could run five years, but with a young person it probably would be the former.

QUESTION: If litigation developed as a result of the injury, would it have any effect on your analysis? Suppose a lawsuit is pending for two years. Would this affect this young man's present condition?

DR. KESSLER: I would not rule out that possibility, but in this particular case I think the massive effect of the injury is the primary factor, and this would continue even after a satisfactory legal settlement.

QUESTION: Is it true that compensation has less effect on younger persons than on older ones? Is it age or athletic prowess that causes you to suggest a minimal effect from compensation in this case?

DR. KESSLER: I referred principally to his being an athlete; his primary difficulty runs in this defect in his body image. I doubt that it will be compensated by money.

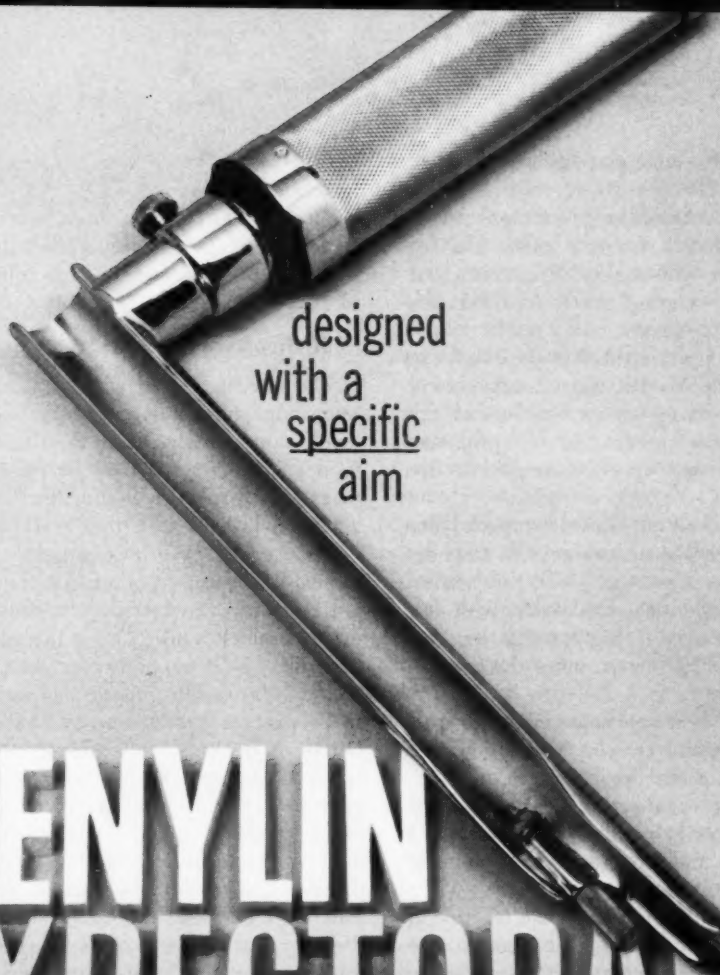
QUESTION: Would you discuss proneness to accidents as a concept and what part it might play in this situation?

DR. SCHIFF: I do not know what part it might play here. We do know that some people, because of an unconscious need to be punished, provoke accidents to their bodies. We see this repeatedly in children, particularly in adolescents, who do all sorts of things because of guilt about the instinctive sexual impulses they have which they feel are wrong. They get into trouble and are punished either physically or psychologically.

QUESTION: In such a case, how does the person explain the way in which he was injured?

DR. SCHIFF: Frequently, it takes a long time before he will tell the doctor how it occurred, even though he may know the doctor already has been told. Finally, when he does tell the story, it is with a great deal of guilt, and he makes statements such as "It was my fault; I'm a terrible person."

(Continued on page A-66)



designed with a specific aim

BENYLIN EXPECTORANT

specifically designed to help control cough

Just as a medical instrument is engineered for maximum efficiency in performing its specific function, BENYLIN® EXPECTORANT is formulated to provide effective relief of cough associated with colds or allergy.

This outstanding antitussive action of BENYLIN EXPECTORANT is attributed to a carefully selected combination of therapeutic agents. Benadryl,® a potent antihistaminic-antispasmodic, reduces bronchial spasm, quiets the cough reflex, and lessens nasal stuffiness, sneezing, lacrimation, itching, and other allergic manifestations. Concurrent respiratory congestion is relieved by expectorant agents that efficiently break down tenacious mucosal secretions. In addition, a demulcent action soothes irritated throat membranes. 59488

BENYLIN EXPECTORANT is a pleasant-tasting, raspberry-flavored syrup... completely acceptable to patients of all ages.

supplied: BENYLIN EXPECTORANT is available in 16-ounce and 1-gallon bottles.

Each fluidounce contains: 80 mg. Benadryl hydrochloride (diphenhydramine hydrochloride, Parke-Davis); 12 gr. ammonium chloride; 5 gr. sodium citrate; 2 gr. chloroform; 1/10 gr. menthol; and 5% alcohol. *Indications:* Relief of coughs due to colds, and other symptoms associated with colds, and coughs of allergic origin. *Dosage:* Adults—1 to 2 teaspoonfuls every three to four hours. Children—½ to 1 teaspoonful every four hours. *Precautions:* Products containing Benadryl should be used cautiously with hypnotics or other sedatives; if atropine-like effects are undesirable; or if the patient engages in activities requiring alertness or rapid, accurate response (such as driving).

PARKE-DAVIS

PARKE, DAVIS & COMPANY, Detroit 32, Michigan

UNIVERSITY OF MICHIGAN LIBRARIES

QUESTION: Do such persons tell the truth about the facts?

DR. SCHIFF: An adolescent will more readily tell the truth than a younger child. The former deals better with reality. Sometimes, telling the truth is a great relief; however, this is not always the case.

QUESTION: I am interested in the comments about the possibility that this case may come up for trial. Getting an evaluation of this man's future treatment and his prognosis might be important in evidence and in the settlement.

DR. KESSLER: I do not know how much value it might be to jurists or attorneys to consider the cost of an average analysis in this matter. If treatment might take five years, with fair chance of success, you might weigh the cost of that treatment in determining the amount of the settlement.

QUESTION: Would you recommend analysis for this young man? Do you feel it would be a definite part of his rehabilitation?

DR. KESSLER: I would recommend it to him, and he would have to make the decision. I would say that analysis would be important for his rehabilitation.

QUESTION: By the success of the treatment, do you mean the ability of the man to live with his defect? He does have a defect in the loss of the eye and facial disfiguration.

DR. KESSLER: Certainly, if he has something he is going to carry with him to his grave, he has to live with that defect and all the related complexes that surround it. Maybe I am being too optimistic about this case, but I believe it would tend to relieve the complexes and any other stirrings of neurosis that were evoked by this injury in the latent part of his neurotic personality.

QUESTION: In other words, you would attempt to minimize the exaggeration or extent of the injury?

DR. KESSLER: That would not be the immediate effect. We would try to bring this personality back into the more normal spectrum, so that he can again have reasonable relations with the world around him and feel comfortable inside without gnawing feelings of unhappiness and pressure.

QUESTION: Would tranquilizing medication have any effect?

DR. KESSLER: If you mean a permanent effect in solving the basic difficulty, I would say no. For helping him over rough periods, of course, it would be helpful.

Medicolegal Solution

The lawyer, armed with legal and medical knowledge, must now resolve this young man's legal claim. The resolution will be made by money payment and may be by an informal private settlement with the tort-feasor or by a formal lawsuit with public adjudication.

The lawyer must evaluate the injuries in this case, bearing in mind that the wrongdoer is liable only (1) for what he caused directly or proximately and (2) for the extent of the disability, be it temporary or permanent. The medical discussion aids the lawyer in placing in proper perspective these two legal issues. Often, as in this case, absolute medical truth is not available. In the areas of medical knowledge as yet undiscovered lie the truthful answers to many current legal questions. Until medical knowledge advances further in the discovery of truthful facts and accurate opinions on the cause and extent of personality disorder, the lawyer in the case presented here must recommend legal solutions without the ultimate in medical aid.

It is interesting to note that over the past several decades the law itself has recognized a change in the causal relationship issue. Originally, it was held that no direct causal relationship between an accident and a personality injury could exist unless a physical blow struck the injured party. If such a physical blow occurred, a personality disorder following it was considered the direct result of the injury. In the absence of such contact, the relationship was indirect, and no damages could be awarded. As medical knowledge has advanced, however, an emotional experience without a physical contact is slowly becoming more acceptable to the law as a direct cause on which to base legal liability. For example, a mother experienced severe psychic shock when she alighted from a bus with her child

(Continued on page A-69)

THERAPEUTIC INDEX Ayerst

MYSOLINE®
BRAND OF PRIMIDONE

IN EPILEPSY

Indications: In the control of grand mal and psychomotor seizures.

Usual Dosage: *Patients receiving no other anticonvulsants—Children under 8 years:* Order of dosage same as for adults, but start with ½ tablet (0.125 Gm.) daily and increase by ½ tablet daily each week, until control. (Where a smaller starting dose is required, use 50 mg. tablet.)
Adults and Children (over 8 years): 1 tablet (0.25 Gm.) daily (preferably at bedtime) for 1 week. Increase by 1 tablet daily each week, until control. Dosage exceeding 2 Gm. daily presently not recommended.

Patients already receiving other anticonvulsants—Children under 8 years: Initially one-half the adult dose, or 0.125 Gm. daily. Gradual increases and decreases as described in adult regimen. (Where a smaller starting dose is required, use 50 mg. tablet.)
Adults and Children (over 8 years): 0.25 Gm. daily, and gradually increased while the dosage of the other drug(s) is gradually decreased. Continued until satisfactory dosage level is achieved for combination, or until other medication is completely withdrawn.

When therapy with "Mysoline" alone is the objective, the transition should not be completed in less than two weeks.

Precautions: Side reactions, when they occur, are usually mild and transient, tending to disappear as therapy is continued or as dosage is adjusted. Commonly reported side effects are drowsiness, ataxia, vertigo, anorexia, irritability, general malaise, nausea and vomiting. No serious irreversible toxic reactions have been observed. (Occasionally, megaloblastic anemia has been reported in patients on "Mysoline." The condition is readily reversible by folic acid therapy, 15 mg. daily, while "Mysoline" is continued.) As with any drug used over prolonged periods of time, it is recommended that routine laboratory studies be made at regular intervals.

Supplied: No. 3430—"Mysoline" Tablets—Each scored tablet contains 0.25 Gm. (250 mg.) of Primidone, in bottles of 100 and 1,000. No. 3431—"Mysoline" Tablets—Each scored tablet contains 50 mg. of Primidone, in bottles of 100 and 500.

Also available: No. 3850—"Mysoline" Suspension—Each 5 cc. (teaspoonful) contains 0.25 Gm. of Primidone, in bottles of 8 fluidounces.

6116

and saw her child run over by the bus as it accelerated too quickly. Personal injury damages for personality disorder were awarded the mother after this incident (Bedenk v. St. Louis Public Service Co., 285 S. W. 2d 609 [Mo., 1955]).

In the present case, the lawyer has a strong argument, for an uncontested physical injury is present and the emotional disorder is severe and reasonably connected to this physical trauma in a direct relationship. The medical prognosis, however, is not so clear. The evidence is weaker on the issue of permanent disability, on which money damages are measured. For this reason, the lawyer would be wise perhaps to recommend a lesser monetary value for settlement and would anticipate a lower jury verdict if litigation ensued. These imponderables are common experiences of the legal practitioner, just as of the medical practitioner. When the practice involves both law and medicine simultaneously, the value of sharing knowledge becomes mandatory. The result may not be an absolute justice, but at least it is a better justice.

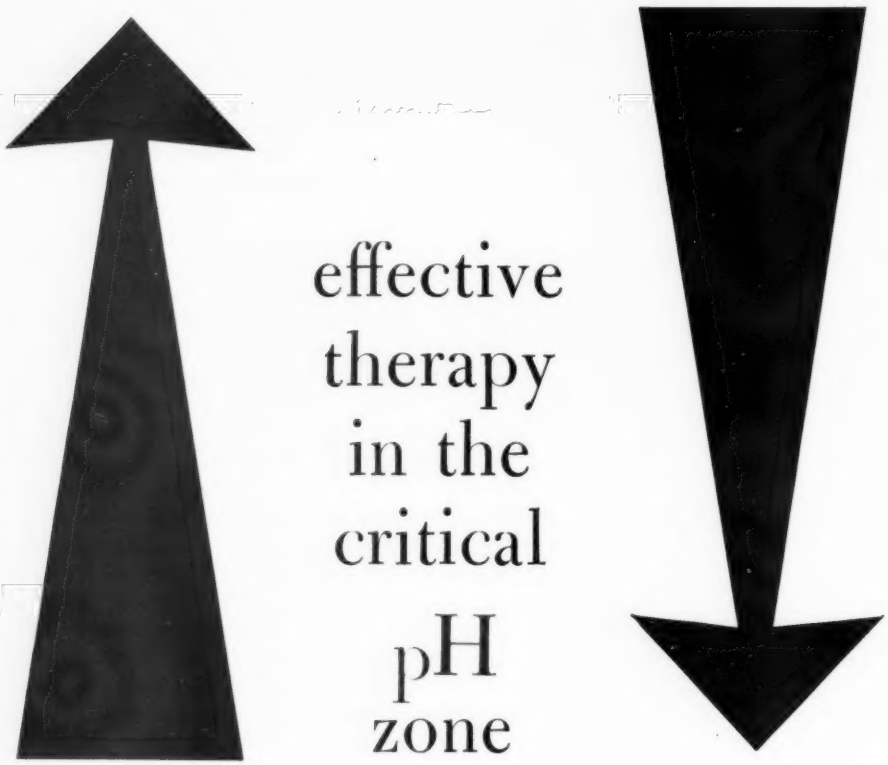
MEETINGS and Postgraduate Courses

HAHNEMANN MEDICAL COLLEGE AND HOSPITAL, PHILADELPHIA: Symposium on recent advances in hypertension to be held May 4-7. For further information, write to: Dr. Albert N. Brest, Head, Section of Hypertension and Renology, Hahnemann Medical College and Hospital, 230 North Broad Street, Philadelphia 2.

TEMPLE UNIVERSITY SCHOOL OF MEDICINE AND HOSPITAL, PHILADELPHIA: Courses for 1961-1962:
Bronchoesophagology, September 11-22, 1961, and January 15-26, 1962
Laryngology and laryngeal surgery, April 2-13, 1962
For further information, write to: Chevalier Jackson Clinic, Temple University Medical Center, 3401 North Broad Street, Philadelphia 40.

UNIVERSITY OF COLORADO MEDICAL CENTER, DENVER: Postgraduate course in clinical and research advances in pediatrics and child guidance problems, to be held August 21-25 at the Stanley Hotel, Estes Park. For further information, write to: Office of Postgraduate Medical Education, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver 20.

UNIVERSITY OF MICHIGAN LIBRARIES



Massengill® Powder

The buffered acid vaginal douche with low surface tension

The normal pH of the vagina (3—4.5) inhibits the growth of most pathogens, but several factors such as menstruation and vaginal infections may cause the vaginal pH to rise . . . thus promoting greater growth of pathogens.

A simple acid douche will restore normal vaginal pH, but it is quickly neutralized by the alkaline mucosa and pH rises again. An effective therapeutic agent must be *buffered* to maintain the pH for several hours and must also be able to *penetrate* the folds of the vaginal mucosa for effective cleansing.

FORMULA: Ammonium Alum, Boric Acid, Phenol, Eucalyptol, Berberine, Menthol, Thymol and Methyl Salicylate.

Radiology FOR PRACTICING PHYSICIANS

Beryllium Disease

PAUL C. HODGES*

Terminology

BERYLLIUM disease is an uncommon, frequently fatal disease caused by the inhalation of even very small amounts of beryllium dust or beryllium salts, possibly triggered by some unknown agent or by intercurrent disease. The terms "berylliosis" and "beryllosis" have been suggested, but the latter seems to connote beryl ore as the causative agent and the former sometimes is applied to all forms of beryllium poisoning and sometimes only to the late or delayed beryllium granulomatosis. Distinction between the acute and chronic forms is not mere pedantry, and failure to make the distinction has led to the misconception[1] that the chelating agents which reduce the toxicity of beryllium injected experimentally into animals might have some therapeutic value in late beryllium granulomatosis of human subjects. It is safer, therefore, to speak of beryllium disease with subdesignation of the type. Hamilton and Hardy,[2] Hardy,[3] Hasterlik[4] and Theodos, Brieger and Cathcart[5] have described both phases of the disease.

*Emeritus Professor and Chairman, Department of Radiology, University of Chicago, Chicago, Illinois.

Beryllium Ore, Metal and Compounds

Man's admiration of emeralds (transparent beryl containing traces of chromium), aquamarine, other gem-quality forms of beryl, and the more common opaque beryl crystals of various shades of green and even yellow is at least as old as the dawn of history, but only during the past three decades has man come to recognize many of the unique properties of the metal and its compounds. Beryllium is an indispensable source of neutrons in physics laboratories and atomic energy plants; it provides strong, thin, heat-resistant and highly radiolucent windows for certain special x-ray tubes. The oxide is an excellent refractory, and alloys of beryllium with copper, aluminum, nickel, magnesium, silver, iron and other metals are characterized by increased toughness, elasticity and resistance to heat and

UNIVERSITY OF MICHIGAN LIBRARIES

tarnishing. In the case of stainless steel, small amounts of beryllium make possible springs that retain elasticity and resistance to corrosion even at a red heat. Obviously, modern technology cannot forego the use of a metal with such qualities as these, but technologists have learned to respect the poisonous nature of beryllium and to employ it only when necessary and then with meticulous care to avoid unnecessary exposure of workers to beryllium dust, fumes or vapors. One of the most toxic forms is zinc beryllium manganese silicate, which in 1938 was first employed as one of the major ingredients for coating the inner surface of fluorescent lamps; since 1949, it has been replaced by other less toxic phosphors.

It has not been possible to designate a dose of beryllium that is safely tolerated, but apparently there is little risk in working ores or alloys containing less than 2 per cent of beryllium metal if reasonable precautions are observed. On the other hand, it has been established that a plant watchman and other workers far removed from actual work with the metal and even inhabitants of nearby houses have acquired the disease, presumably from inhaling fumes from plant stacks. Hasterlik stated that air concentrations as low as 25 millionths of a gram per cubic meter of inspired air are dangerous, so obviously the aim should be to avoid any inhalation of beryllium whatever.

Acute Beryllium Pneumonia

In Germany, Italy and Russia, it was noted as early as 1933 and 1935 that workers extracting metal from beryllium ore were subject to acute pneumonia which cleared when exposure to beryllium stopped; however, the condition was not recognized in the United States until 1938, and the earliest American publication of it was in 1943. The symptoms and x-ray changes which appear within days or even hours following exposure resemble those of any acute pneumonia and, if exposure is terminated, yield to the usual therapeutic measures. Approximately 8 per cent of patients die, however, and, in approximately a third of those who recover, the delayed form develops six months or as much as six years later, even in the absence of further exposure to beryllium.

Delayed Beryllium Granulomatosis

Although many body tissues are involved in this disease, the lung lesions usually are the first to attract the attention of the patient and his physician. Radiologically, these pulmonary lesions resemble sarcoidosis so closely that differentiation is difficult, if not impossible, and some have even argued that sarcoidosis is, in fact, berylliosis. Clinically, patients exhibit the symptoms of oxygen deficit, and this and the x-ray findings are explained by the histology. Proliferation of pulmonary epithelium is so severe that many of the alveoli are obliterated, and at autopsy lesions are also found in the liver, lymph nodes and other tissues. In addition, spectroscopic analysis shows a storage of beryllium in all these sites, particularly in the bones.

Patients long recovered from the acute phase may remain well until intercurrent illness, surgery, pregnancy or (in one case) a cutaneous granuloma developing about a splinter of beryllium in the skin precipitates the delayed form. It has been suggested that the precipitating mechanism may be mobilization into the blood stream of beryllium previously stored in the bones, rendering it free to act on body tissues that had been sensitized during the acute pneumonic phase months or even years earlier. There is no known specific treatment, but antibiotics do control intercurrent infection and a maintenance dosage of cortisone is of major help in some cases. Regardless of the type of therapy, however, about a third of the patients die and half of those who survive become invalids.

X-ray Diagnosis

One must say here, as in so many other conditions, that whereas the x-ray examination frequently gives the first intimation that pulmonary lesions are present and is of major importance in arriving at the diagnosis it is not in itself diagnostic. The diagnostic criteria are best considered in connection with the following five cases used as illustrations.

Case 1—Ten years before we examined a

43 year old clerk, he had worked for only four months in an office adjacent to a room in which defective fluorescent lamps were broken up for junking. Subsequently, a partial pneumothorax developed in this patient, accompanied by loss of weight and dyspnea. By the time we saw him, the diagnosis had been established by chemical examination of tissue obtained at biopsy. The x-ray findings (figure 1) were compatible with beryllium granulomatosis but in themselves by no means ruled out several other possibilities. Three and one-half years later, the patient died in heart failure, and autopsy confirmed the diagnosis of beryllium disease.

Case 2—At the age of 35, a man had a normal chest film at pre-employment examination. Two years later he complained of fever, fatigue, cough, chest pain and loss of weight; the referral diagnosis was tuberculosis(?) or neoplasm(?). At x-ray examination (not shown here) we reported the heart to have a mitral shape and to be 40 per cent oversized for build. We noted a small infiltrate in the base of the right lung, the nature of which was not determined. Four years after the patient's employment and two years after the onset of symptoms, our film (figure 2a) was interpreted as showing cardiac enlargement and marked increase in the infiltration in the right lung base, which we thought probably represented bronchiectasis. The heart continued to enlarge, and clinically and radiologically it was concluded that the cardiac lesion was rheumatic valvulitis and that the increasing densities in both lung bases represented hemosiderosis. Finally, seven years after the onset of symptoms (figure 2b), it was established that the patient had beryllium disease which had been acquired in the course of wartime work in the field of nuclear physics and atomic energy. In retrospect, the cardiac lesion was secondary cor pulmonale, but, fortunately, in spite of the cardiac damage and the extensiveness of lung involvement, the patient has done well on cortisone therapy.

Case 3—At his initial examination, a 37 year old man gave a history of dyspnea and weight loss during the previous three months; the referral diagnosis was sarcoidosis(?).

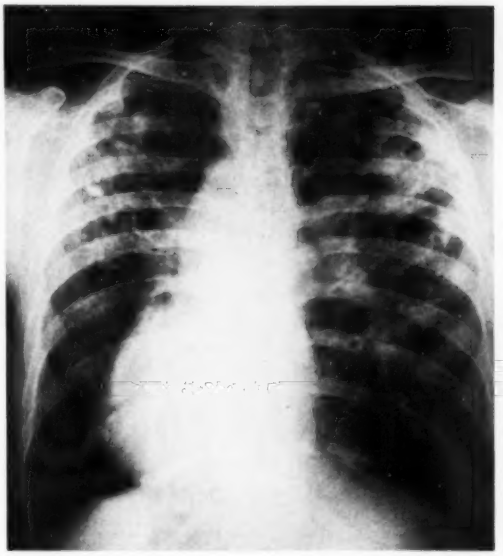


FIGURE 1. Fatal delayed beryllium granulomatosis in a man who was employed briefly 10 years earlier in a fluorescent lamp factory.

Seven months later, pulmonary infiltration had increased, and there was emphysema of the lung bases (figure 3). Shortly after this, we learned that nine years before the onset of symptoms the patient had worked for about a year mixing phosphors at a fluorescent lamp factory. It was not possible to determine whether or not he had had acute beryllium pneumonia during the period of exposure.

Case 4—Acute pneumonia developed in a 22 year old chemist within four months after he had been exposed to beryllium in wartime atomic energy work. Since at that time the toxicity of beryllium was not recognized in this country, the nature of the pneumonia in this patient was not understood, and only by accident did he escape further exposure during the next two years. After a lapse of two years, he was exposed again for two years, and when delayed beryllium granulomatosis developed five years after his initial employment the disease was rapidly fatal. Figure 4a is the chest film made at pre-employment examination; it shows no pathologic condition. Figure 4b was made several months after the onset of the granulomatosis and five months

UNIVERSITY OF MICHIGAN LIBRARIES

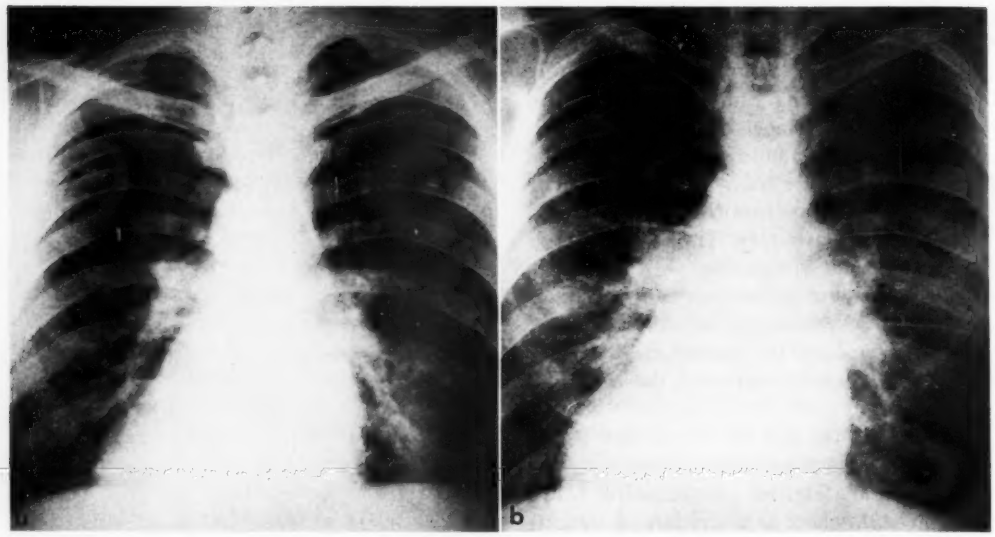


FIGURE 2. a. Delayed beryllium disease in a war plant worker. At the time this x-ray was made, it was not known that the patient had been exposed to beryllium; the cardiac enlargement was considered primary, and the lung infiltrate was thought to be hemosiderosis.

b. An x-ray of the same patient made five years later, which was seven years after the onset of symptoms.

before death; it shows bilateral pulmonary infiltration, more extensive on the right than on the left side.

FIGURE 3. Severe delayed granulomatosis in a man who had been exposed to beryllium phosphor nine years earlier while working in a lamp factory. This x-ray was made four months after the onset of symptoms.

Case 5—A 20 year old man was referred to us with a history of productive cough, fever, fatigue and loss of weight. At our first examination (figure 5a) our interpretation was bilateral pulmonary tuberculosis with partial pneumothorax on the left side. He was treated in a sanatorium, but when no tubercle bacilli could be found it was assumed that he had sarcoidosis. By the time of our third examination (figure 5b), it had been discovered that five years earlier the patient had worked in a fluorescent lamp plant, and the diagnosis of delayed beryllium granulomatosis had been established. The pneumothorax and some of the pulmonary lesions have disappeared, undoubtedly because secondary infection had been brought under control. With avoidance of further intercurrent infection and judicious use of cortisone, the prognosis is fairly good.

Prophylaxis

Edward Jenner discovered smallpox vaccination in 1796, but 65 years later Henry Gray, author of "Gray's Anatomy," died at the age of 34 of smallpox acquired from one

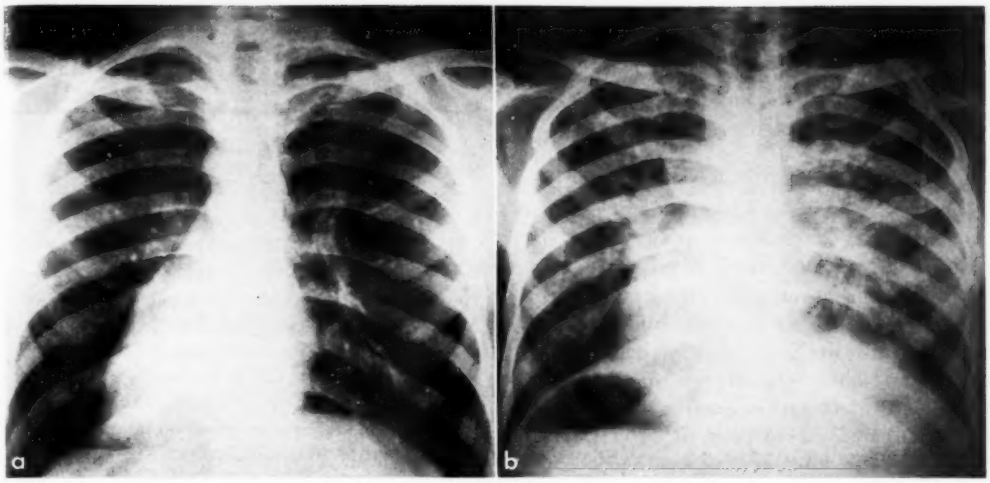


FIGURE 4. a. Pre-employment chest x-ray showing normal findings in a 22 year old chemist.

b. In the same patient, severe, rapidly fatal beryllium granulomatosis developed five years after he had been exposed to beryllium. This x-ray was made four and three-fourths years after the acute phase of the disease.

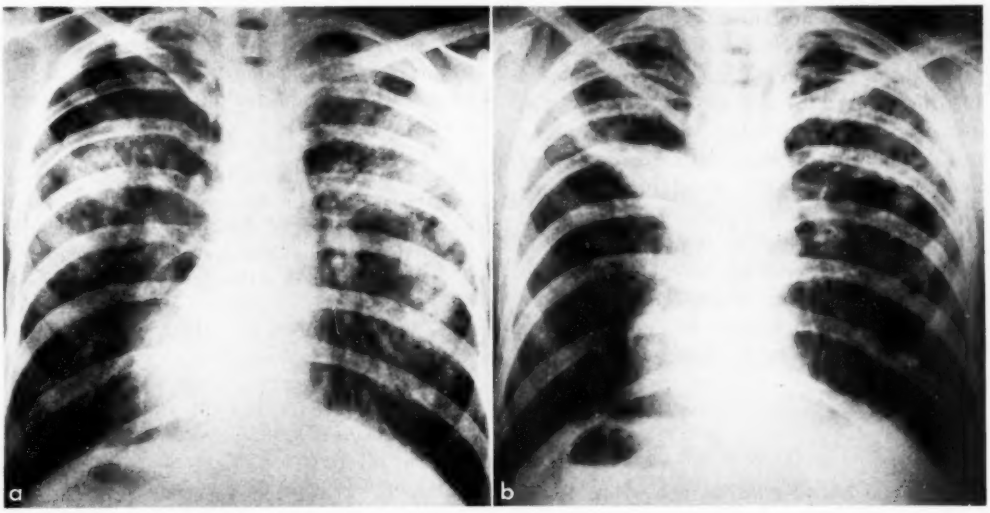


FIGURE 5. a. Beryllium granulomatosis complicated by intercurrent infection and partial pneumothorax on the left side. This was mistaken for pulmonary tuberculosis.

b. One year later the secondary infection had been controlled and it had been established that the patient was exposed to beryllium phosphor five years before the x-ray shown in figure 5a had been made.

of his patients. Trench foot caused much disability and misery in World War I soldiers until their medical officers identified it as frostbite and insisted that waterproof boots and dry socks be given priorities equal to those of food and ammunition. The lesson,

UNIVERSITY OF MICHIGAN LIBRARIES

however, had to be learned all over again some 35 years later in Korea.

Teachers of toxicology and the larger users and processors of beryllium are alert to its toxicity and aware of the means available for protecting those who process the ore or the metals. However, beryllium alloys are now widely used, and there is constant risk that even with alloys containing as little as 2 per cent beryllium new methods of processing may result in concentration or in increased inhalation, ingestion or absorption to dangerous levels. Within the year, while visiting the experimental laboratory of one of America's leading manufacturers of electronic equipment, I saw an acid bath for etching bronze sheet. As I suspected, the bronze contained a small amount of beryllium, but it had not occurred to the chief of the laboratory to inquire as to the amount of beryllium present in the bronze or the extent to which it might accumulate in the etching bath or in the vapors arising from it.

All physicians are aware of the toxicity and are alert to the ever-present possibility of heavy metal poisoning. Now they must learn that the lightest of the metals also is toxic, and on being confronted with acute pneumonias or lesions resembling sarcoidosis they must keep in mind the possibility that they may be dealing with beryllium disease. Not only will early detection improve the prognosis of such patients but, even more important, it may uncover unsuspected beryllium hazards in local laboratories or manufacturing plants and, by flagging the danger, save others from exposure.

REFERENCES

1. Schubert, J.: Beryllium and berylliosis. Scient. Am. 199:27-33 (August) 1958.
2. Hamilton, A. and Hardy, H. L.: Industrial Toxicology. Ed. 2. New York, Paul B. Hoeber, Inc., 1949, pp. 172-187.
3. Hardy, H. L.: The disability found in persons exposed to certain beryllium compounds. A.M.A. Arch. Indust. H. 12:174-181 (August) 1955.
4. Hasterlik, R. J.: Beryllium poisoning. Phys. Today 2:14 (June) 1949.
5. Theodos, P. A., Brieger, H. and Cathcart, R. T.: Chronic pulmonary beryllosis. J.A.M.A. 158:1428-1429 (August) 1955.

The Editor's Mail

SUBACUTE DIFFUSE THYROIDITIS

To the Editor:

Dr. Alvin L. Schultz, in his excellent presentation on the treatment of subacute diffuse thyroiditis in the January issue of Postgraduate Medicine, said that "The therapeutic response to TSH in our three cases was not impressive," and "One patient (R.C.) became worse following administration of TSH, with increase in thyroid pain, weakness, fever and malaise."

I should like to emphasize that such a reaction from the administration of TSH could have been expected, because during the acute phase of thyroiditis the main purpose of treatment is to quiet the thyroid which is in turmoil and not to stimulate it with TSH. For this reason, it is necessary to suppress the function of the hypophysis, especially the secretion of TSH.

Thus, in treating thyroiditis, the use of a thyroid substance (PROLOID®) plus an antiinflammatory steroid (dexamethasone) and, in the beginning of treatment, an antibiotic (tetracycline) is rational.

In 14 of our cases, these drugs were used concomitantly in the following manner with very good results: (1) tetracycline (COSA-TETRACYN®), 4 capsules of 250 mg. each per day for five days, (2) dexamethasone (DECADRON®), 0.75 mg. four times a day for four to five days, then in diminishing dosages for about two weeks, and (3) Proloid, 0.03 gm. (½ gr.) three or four times a day for two months or more.

In four cases, dexamethasone was not administered because the patients either had a history of or had duodenal ulcer. The therapeutic results were equally good but less dramatic.

Our opinion is that in treating subacute diffuse thyroiditis the administration of a thyroid substance (Proloid) is *sine qua non*, and the concomitant administration of steroids (dexamethasone, etc.) and antibiotics (tetracycline) as adjuvants is useful. With this treatment, the patient's recovery is complete and without any sequelae.

Sincerely,
L. G. Polymenakos, M.D.
Toronto, Ontario

his first cereal...

like his first formula...needs your guidance

PABLUM®

mother looks to you

Baby's first cereal can be his introduction to adult eating—an experience which can help set good eating habits for the rest of his life. Mother looks to you for help in making the right diet choices for her infant. Your advice is as important as it was when you prescribed his first formula.

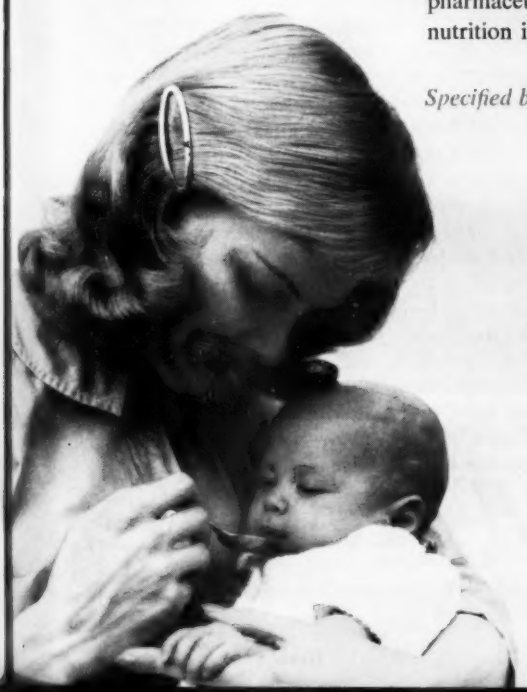
meets baby's needs at this critical point

PABLUM brand cereals are formulated especially to fill the infant's needs for important minerals—especially iron—and for proteins, vitamins, carbohydrate, and calories. Available in five varieties—Rice, Mixed, Oatmeal, Barley, and High Protein—PABLUM cereals are highly useful in taste training.

your assurance of nutritional excellence

Mead Johnson applies the same rigorous controls to the manufacture of PABLUM cereals as it does to its other nutritional products and its pharmaceuticals. Your specification of PABLUM is assurance of sound nutrition in cereals for your patients' first few years.

Specified by physicians for nearly 30 years.



Edward Dalton Co.
A DIVISION OF
MEAD JOHNSON & COMPANY

Quality products from nutritional research

45361

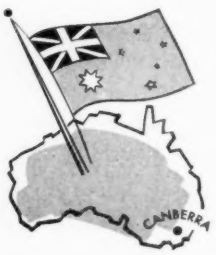
UNIVERSITY OF MICHIGAN LIBRARIES

Medicine from Abroad

FROM POSTGRADUATE MEDICINE'S CORRESPONDENTS

ARGENTINA: ISAAC BERCONSKY, M.D.
AUSTRALIA: GRAYTON BROWN, M.D.
AUSTRIA: M. ARTHUR KLINE, M.D.
BRAZIL: A. BRICKMANN, M.D.
DENMARK: TORBEN JERSILD, M.D.
ENGLAND: R. SCOTT STEVENSON, M.D.
FINLAND: LEO NORO, M.D.
FRANCE: JEAN MEYER, M.D.
GREECE: NICK J. PHOTINOPOULOS, M.D.
ISRAEL: RAFAEL J. SCHEN, M.B.
JAPAN: HARUTO UCHINO, M.D.
SPAIN: MRS. EDITH BULSON

AUSTRALIA



Harelip and cleft palate in Tasmania—In the *Medical Journal of Australia*, Dr. B. K. Rank, consulting plastic surgeon, Tasmania, and Mr. J. A. Thomson, University of Melbourne, Melbourne, have reported their observations on 160 patients with harelip or cleft palate or both, all of whom were born in Tasmania during the years 1945 to 1957, inclusive. One of every 600 children born in Tasmania has a harelip or cleft palate or both; of these, 32.5 per cent have a family history of this defect. Harelip and cleft palate are prevalent throughout all districts of Tasmania, and occur with equal frequency in rural and urban areas. A significant number of children with these anomalies are born to mothers in the older age groups. Because of this high incidence, it would seem unwise to permit immigrant families who are known to carry this trait to be freely admitted to this community.

In examining the hereditary basis for these defects, the authors concluded that, contrary to the currently accepted view of Fogh-Andersen, harelip with or without cleft palate is not always caused by a genetic system independent of that producing cleft palate alone. However, at least two main genetic complexes are involved; one or more dominant genes of reduced manifestation probability are responsible in each case.

The history of its settlement indicates why Tasmania has such a high incidence of mental retardation and congenital malformation. In addition to its natural increase, the population of this island (333,000) has been augmented by continuous European immigration from the time of the first settlement of Van Diemen's Land in 1803. The difficulties of travel and the relative isolation of pioneer family groups provided conditions conducive to intermarriage among the early settlers. The more progressive and intellectual people have since moved from the island community to find better opportunities on the Australian mainland. Scott (1957) stated that this immigration from outlying areas to the cities or the mainland "robbed the rural areas, especially the inhospitable hill country, of much of their able youth, leaving behind the less able, amongst whom in many isolated areas intermarriage has bred a feeble-minded stock."

(Continued on page A-92)

Put your low-back patient back on the payroll

Soma relieves stiffness —stops pain, too

YOUR CONCERN: Rapid relief from pain for your patient. Get him back to his normal activity, *fast!*

HOW SOMA HELPS: Soma provides direct pain relief while it relaxes muscle spasm.

YOUR RESULTS: With pain relieved, stiffness gone, your patient is soon restored to full activity—often in days instead of weeks.

Kestler reports in controlled study: *Average time for restoring patients to full activity: with Soma, 11.5 days; without Soma, 41 days.* (*J.A.M.A. Vol. 172, No. 18, April 30, 1960.*)

Soma is notably safe. Side effects are rare. Drowsiness may occur, but usually only in higher dosages. Soma is available in 350 mg. tablets. **USUAL DOSAGE: 1 TABLET Q.I.D.**

The muscle relaxant with an independent pain-relieving action

SOMA®

(*carisoprodol, Wallace*)

Wallace Laboratories, Cranbury, New Jersey

BRAZIL

Typhoid fever—In the *Revista do Hospital das clínicas da Faculdade de medicina da Universidade de São Paulo,* Dr. G. Del Negro has reported on a clinical study of 60 children with typhoid fever who were treated in the infectious diseases department of the Hospital das clínicas, São Paulo, during the period from January 1952 through September 1959. Their ages ranged from 3 to 15 years. Data concerning the clinical picture, results of physical examination, laboratory findings, treatment, and general course of the disease were analyzed.

The onset of typhoid fever was usually abrupt, and a remittent or even intermittent type of fever was observed in the benign cases. There was no dicrotism. Diarrhea was frequently observed, but intestinal hemorrhage was rare. There was perforation of an intestinal ulcer in 10 per cent of the patients.

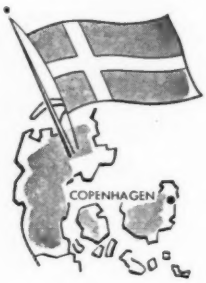
Splenomegaly was present in approximately 75 per cent of these patients. Benign pulmonary complications (bronchitis) occurred in about 30 per cent. Psychotic disturbances (mental distress, dullness, stupor) were much less frequently observed than was a normal mental status.

Bone-marrow culture was sometimes valuable in diagnosis. The mean duration of illness before admission to the hospital was 12 days; 53 per cent of the blood cultures taken at the time of admission gave positive results. The Widal agglutination test was found to be the most useful routine diagnostic procedure, giving positive results in 51 of 58 cases in which it was carried out one or more times. Leukopenia (less than 5000 white blood cells per cubic millimeter) was evident in 13.3 per cent of the patients; the white blood cell count was normal in 48.3 per cent.

A majority of the patients in this series (80 per cent) had eosinopenia (disappearance of eosinophils from the peripheral blood); in only two cases was the eosinophil count above 400 per cubic millimeter. The coexistence of worm infestation did not affect the decrease of eosinophils in the acute stage of the disease; however, in patients infested with *Schistosoma mansoni,* a normal eosinophil count or even eosinophilia was usually seen.

Complications, which occurred in 10 patients, included perforation of an intestinal ulcer (seven), septicemia (two), and intestinal hemorrhage (one). All but four of the patients were treated with the specific antibiotic chloramphenicol and with surgery if necessary. One of these four patients died before treatment was begun; three recovered without antibiotic therapy. Of the 60 patients in the series, 56 recovered and four died.

DENMARK



Cholelithiasis—In the *Danish Medical Bulletin* Drs. Ib Andersen, P. Thestrup Andersen, Thue Poulsen and Bent Rasmussen have reported on a series of 1,673 patients operated on for cholelithiasis during the period 1937 to 1957. The majority of these patients were from 40 to 60 years of age. In the group in which ages ranged from 10 to 30 years, the ratio of male patients to female patients was 1:16, and, in the group of patients from 30 to 40 years old, it was 1:6; the over-all ratio was 1:3.8. About 97 per cent of these patients had calculi.

In 1937 surgery on the biliary tract accounted for 1.3 per cent of all operations performed, and in 1957 for 4.5 per cent. In the latter half of this period there were fewer cases of cholelithiasis with complications and inflammation than in the first half. The incidence of complications was higher among men than among women, and there was no correlation between inflammatory complications and duration of illness.

Biliary obstruction occurred in patients with simple cholecystolithiasis more often than was expected, and it was seen more frequently in women than in men. It was most common in patients in whom the disease was complicated by cholecystitis or choledocholithiasis.

The operative rate increased from 40 to 80 per cent during this period. Operative indications were extended to include everything but resting gallstones, and many contraindications for surgery were eliminated. Emergency operations were performed only when necessary. The introduction of operative cholangiography led to a pronounced decrease in the number of explora-

(Continued on page A-94)

PATHIBAMATE 200 400

for
real or potential
ulcer...

PATHIBAMATE®

meprobamate with PATHILON® tridihexethyl chloride Lederle

anticholinergic . . .
treats the trauma

tranquilizer . . .
controls the tension

Indications: duodenal ulcer; gastric ulcer; intestinal colic; spastic and irritable colon; ileitis; esophageal spasm; anxiety neurosis with gastrointestinal symptoms, and gastric hypermotility.

Administration and Dosage: PATHIBAMATE-400 (full meprobamate effect)—1 tablet three times a day at mealtime, and 2 tablets at bedtime. PATHIBAMATE-200 (limited meprobamate effect)—1 or 2 tablets three times a day at mealtime, and 2 tablets at bedtime. Adjust to patient response.

Contraindications: glaucoma; pyloric obstruction, and obstruction of the urinary bladder neck.

Lederle

LEDERLE LABORATORIES
A Division of AMERICAN CYANAMID COMPANY
Pearl River, New York

UNIVERSITY OF MICHIGAN LIBRARIES

tory choledochotomies and to a larger number of uncomplicated cholecystectomies. Positive findings revealed by choledochotomy increased from 35 to 70 per cent during this period. There also was a small increase in the number of positive findings in the deep bile ducts.

The incidence of complications following operation for cholecystolithiasis and cholecystitis decreased, while the number of complications following operation for choledocholithiasis increased, presumably because of the more frequent use of a common duct drain.

Mortality was twice as high among men as among women, and was highest in older patients and in patients with complications. In 33 per cent of these patients, autopsy revealed overlooked calculi in the deep bile ducts, and in 35 per cent technical errors or mishaps were the cause of death. Operative injuries occurred in a total of five patients (0.3 per cent) and caused one death. The mortality dropped from about 10 per cent in 1937 to about 1 per cent in 1957. The over-all mortality was 2.6 per cent.

ENGLAND

Fractures of the malar bone—In a recent discussion at the Royal Society of Medicine, Air Commodore George H. Morley, surgeon to the Royal Air Force, said that fractures of the malar or zygomatic bone may be disguised by edema until it is too late to reduce them easily. Fracture displacements of the body may displace the globe of the eye or simply upset its power of convergence. The zygomatic arch can obstruct the coronoid process of the mandible and eventually prevent movement of the jaw (trismus). Involvement of the infraorbital nerve numbs the cheek and upper lip. Yet, despite these symptoms, a fracture often is not diagnosed or is considered to "require no treatment." A subconjunctival hemorrhage continuous to the lower fornix and an unexpected opacity of the maxillary antrum should indicate closer inspection of the x-rays and the patient to detect the fracture.

In most cases reduction is simple, performed by the subfascial temporal leverage devised by Gillies. Less frequently, it is necessary to reduce by opening and packing the antrum, but it rarely has been found necessary to resort to pins and wiring to secure reduction. As a result of his experience with 93 cases, Air Commodore Morley advises reduction when in doubt. Occasionally, a tardy infraorbital neuralgia develops in unreduced cases, requiring a tricky decompression of the canal.

Drugs in treating depression—Dr. William Sargant, psychiatrist, St. Thomas's Hospital, London, has pointed out in the *British Medical Journal* that depressive illnesses are now the most easily treated and have the highest potential for recovery of all types of mental illness. Patients who have atypical or hysteric depression and who previously had good personalities may show remarkable improvement after even a few days of treatment with the new antidepressant drugs.

Iproniazid (MARSILID®) is one of the most effective of the monoamine oxidase inhibitors, but the danger of a severe toxic jaundice in one of every 250 patients makes the use of this drug undesirable, except with special precautions. Dr. Sargant has found that a dosage of either 15 mg. phenelzine (NARDIL®) or 10 mg. isocarboxazide (MARPLAN®) three or four times daily is the safest and the most practical, efficacious treatment for general use; however, neither drug is as effective as iproniazid. He has not found nialamide (NIAMID®) to be as good as phenelzine or isocarboxazide in the type of cases described. Although pheniprazine hydrochloride (Cavodil) can be effective, its complications seem greater and it can be more disturbing to the patient than phenelzine or isocarboxazide.

Another of the new and widely publicized antidepressant agents, imipramine (TOFRANIL®), is not an amino oxidase inhibitor; it is more closely allied with the chlorpromazine (LARGACTIL®) group of drugs. On the whole, it is most effective in the more endogenous types of depression, but is of less value in the neurotic depressions. It also generally takes longer to work. The necessary dosage may vary from 25 to 75 mg. three times daily, and it undoubtedly can alleviate attacks in some of the milder cases of endogenous depression without electroshock therapy.

Treatment of spinal injuries—Mr. Robert Roaf, lecturer on orthopedic surgery at the University of Liverpool Medical School, has pointed out in a recent issue of the *Lancet* that considerable advances have been made in the treatment of irreversible quadriplegia after severe cervical injuries. With the greater speed of automobiles

(Continued on page A-96)

***FIBRINOYLSIN**—to provide active enzyme for fibrin substrate debridement—**DESOXYRIBONUCLEASE**—to lyse desoxyribonucleic acid in degenerating leukocytes and other nuclear debris.*

Since ELASE provides, not a precursor, but an active enzyme,[1] it quickly lyses fibrinous material in serum, clotted blood, and purulent exudates. It does not, however, attack living tissue to any appreciable degree, nor does it have an irritating effect on granulation tissue in wounds.[1-4]

Good results have been obtained with ELASE in the debridement of infected surgical wounds.[1-4] Exudative lesions that have responded well include second- and third-degree burns, ulcerations, small gangrenous areas of the extremities, sinus tracts, fistulas, abscess cavities (including empyema), wounds, and pyodermas. Prompt and striking symptomatic relief has also been obtained in patients with gynecologic complications.[4]

ELASE (fibrinolysin and desoxyribonuclease, combined [bovine], Parke-Davis). Dry material for solution, each vial contains 25 units (Loomis) of fibrinolysin and 15,000 units of desoxyribonuclease with 0.1 mg. thimerosal as a preservative. Ointment, tube of 30 grams containing 30 units (Loomis) of fibrinolysin and 20,000 units of desoxyribonuclease with 0.12 mg. thimerosal in a special petrolatum base; tube of 10 grams containing 10 units (Loomis) of fibrinolysin and 6,666 units of desoxyribonuclease with 0.04 mg. thimerosal in a special petrolatum ointment base. *Indications:* To lyse fibrin and liquefy pus. Aid in removal of necrotic debris associated with vaginitis and cervicitis. Useful in the removal of exudate from skin surfaces as in wounds, ulcers, burns; also used to irrigate abscess cavities, superficial hematomas, sinus tracts, fistulas. *Dosage:* Apply topically as ointment or solution. Intravaginally—in mild to moderate vaginitis and cervicitis, deposit 5 cc. of ointment deep in the vagina once nightly after retiring for five applications; re-examine for possible need of further therapy. In more severe cervicitis and vaginitis, 10 cc. of solution may be initially instilled intravaginally, waiting one or two minutes for dispersal, then inserting a cotton tampon to be removed the next day, followed by as many applications of ointment as necessary. Skin surface lesions—topically, as indicated. After application, enzymatic activity becomes rapidly and progressively less and is probably exhausted for practical purposes at the end of 24 hours. The ointment and dry material for solution are stable at room temperature for a period of one year. *Precaution:* Not for parenteral use; bovine fibrinolysin may be antigenic. Side effects are minimal, consisting usually of local hyperemia. Observe usual precautions against allergic reactions, particularly in persons highly sensitive to materials of bovine origin.

PACKAGE INFORMATION: ELASE is supplied as an ointment in 30-Gm. and 10-Gm. tubes. Disposable vaginal applicators (V-Applicators) for application of ointment are available separately in packages of 6. ELASE is also supplied as lyophilized powder in rubber-diaphragm-capped vials. To be maximally effective, the solution must be freshly reconstituted with isotonic sodium chloride just prior to topical use. Within six hours after preparation, half of its potency is lost at room temperature.

FEB. 1961 (P-546)

PARKE-DAVIS

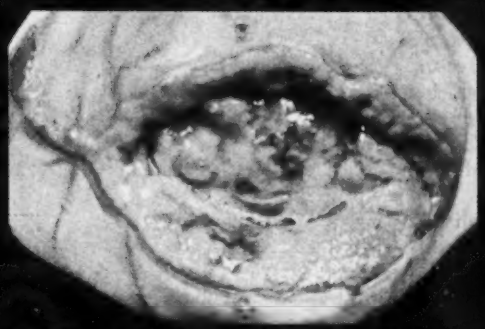
PARKE, DAVIS & COMPANY, Detroit 32, Michigan

in infected surgical wounds... a rational approach to therapy

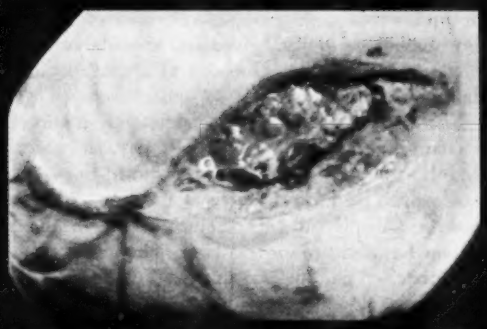
Elase

FIBRINOLYSIN AND DESOXYRIBONUCLEASE, COMBINED, (BOVINE), PARKE-DAVIS ®

purulent amputation stump with osteomyelitis, left leg of 12-year-old boy



Draining wound four weeks postoperatively and prior to enzymatic therapy. Infective organisms identified were Pseudomonas and coagulase-positive staphylococci.



Eight days later. Solution containing 50 Loomis units fibrinolysin and 50,000 units desoxyribonuclease applied topically, for periods of three hours 3 times daily, for seven days. Considerable improvement in fibrinopurulent base of stump.

REFERENCES: (1) Coon, W. W.; Wolfman, E. F., Jr.; Foote, J. A., & Hodgson, P. E.: Am. J. Surg. **98**:4, 1959. *(2) Friedman, E. A.; Little, W. A., & Sachtleben, M. R.:* Am. J. Obst. & Gynec. **79**:474, 1960. *(3) Margulis, R. R., & Brush, B. E.:* Arch. Surg. **65**:511, 1952. *(4) Personal Communications to the Department of Clinical Investigation, Parke, Davis & Company, 1959.*

UNIVERSITY OF MICHIGAN LIBRARIES

and the more frequent wearing of crash helmets by motorcyclists, the incidence of such injuries is increasing. In the early stages, patients are likely to die from respiratory embarrassment, but a timely tracheostomy and the use of a Tunnicliffe jacket respirator will save most of them. Another early complication is intestinal ileus. Gastric suction and intravenously administered fluids will tide most patients over this period.

If these patients survive the early stages and if bedsores and urinary infection are avoided, the prognosis for life in quadriplegics is good.

FRANCE

Delayed healing in fractures—The successful treatment of fractures in which healing had been delayed has been reported in *La Presse médicale* by Drs. M. Isélin, P. Gonnard and D. Benoist. Their series included 34 patients in whom fractures had failed to heal within 68 days to 21 months. Sites of the fractures included the legs, thighs, femoral neck, clavicle, fingers, etc.

Invariably, electrophoresis of the blood serum of these patients demonstrated some irregularity. The irregularities consisted of an over-all excess of delta$_2$-globulin or of an excess of alpha$_2$-globulin or gamma-globulin. All fractures healed within three weeks with the administration of 15 mg. dexamethasone daily (given in three doses) for 17 days, followed by a dosage of 25 mg. ACTH daily for three days.

The normal process of cicatrization involves a change at about the twentieth day, at which time the blood circulation slows down, the acid-base equilibrium of the focus changes to alkaline, and the phosphorus and calcium present become fastened in the protein matrix of the callus. The fracture then calcifies and heals.

Delay in healing may be caused by the persistence of increased vascularization and the accompanying acid pH, which hinders the setting of the phosphorus and calcium. Electrophoresis will demonstrate the presence of a protein-globulin imbalance. Ordinarily, cortisone inhibits scar formation in fractures; however, in cases such as those described, its antiphlogistic and catabolic properties will force the increased vascularization to abate and will permit rapid healing.

The need for performance of electrophoresis is stressed, since it is not always possible to differentiate clinically between a delay in healing caused by disturbed protein-globulin balance, which is curable by cortisone, and a pseudarthrosis with normal electrophoresis, which requires surgery.

Qualitative deficiencies in immunity—In *La Presse médicale*, Drs. R. Cattan and P. Vésin have described a syndrome which involves frequent intestinal febrile episodes, recurring over a period of years and accompanying various infections, including otitis media, sinusitis, staphylococcal skin infections, and innumerable colds.

Laboratory examinations reveal paradoxically normal or slow sedimentation rates in patients with this syndrome. Electrophoresis demonstrates a moderate decrease in gamma-globulin, and immunoelectrophoresis indicates a decrease in the beta$_2$-M and beta$_2$-A globulins.

The level of circulating antibodies (especially antistreptolysin 0) is lowered, particularly at the time of active infection, when it drops to 50 to 100 units instead of the normal 300. T.A.B. inoculation provokes a normal reaction to H antigen but no reaction to 0 antigen.

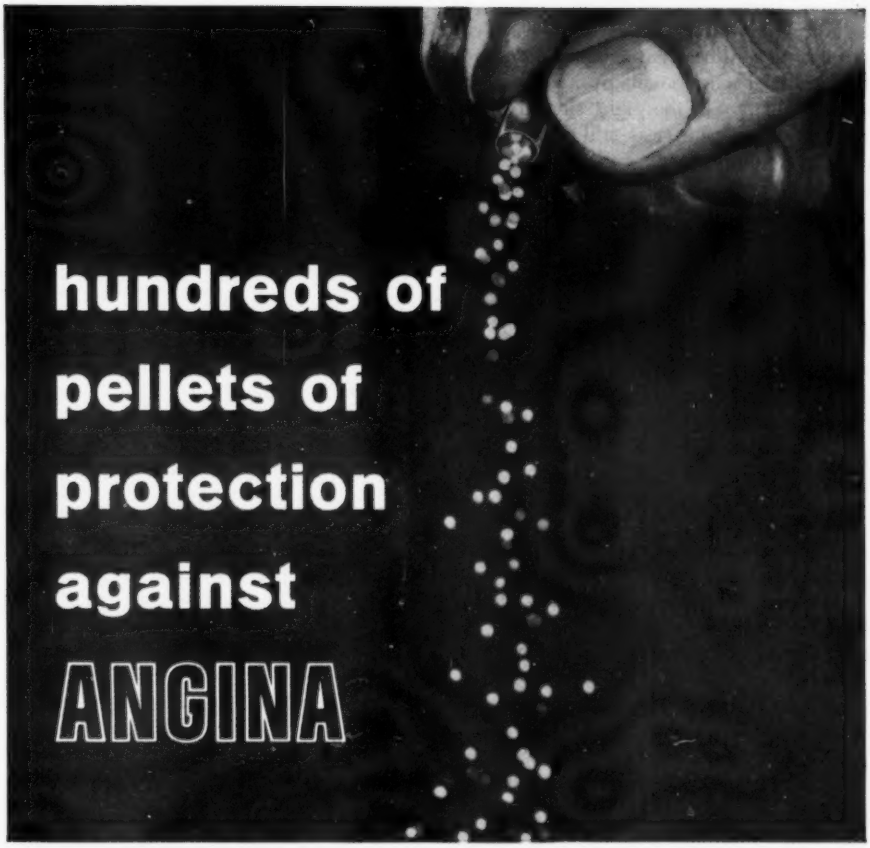
This condition evidences a qualitative deficiency in immunity which is not related to any considerable drop in the level of beta-globulin and of gamma-globulin but to a failure in antibody production after antigenic stimulation. The mechanism involved is obscure.

Injections of gamma-globulin will correct the deficiency. The required dosage is 20 ml. globulin (about 3 to 5 gm. gamma-globulin and an indefinite amount of beta$_2$-globulin) every 20 days for several months.

ISRAEL

Radioiodine in the diagnosis of myocardial infarction—Radioiodine is taken up selectively by necrotic heart muscle and thus can be utilized in diagnosing myocardial infarction. In the *Israel Medical Journal*, F. Dreyfuss, A. Hochman, M. Ben-Porath and J. Menczel have reported the results of a preliminary study of nine patients

(Continued on page A-98)



PENTRITOL® TEMPULES

controlled disintegration capsules

A single 30 mg. Pentritol Tempule with 12 hour action exhibits an even nitrite release which "tends to produce a smooth, prolonged response similar to that of the sustained release of modern depot injections."[1] Duration, frequency, and severity of anginal attacks are markedly lessened. Patients showing little progress during years of therapy with 80 mg. daily of PETN tablets, respond favorably to the smaller dose of Pentritol Tempules.[2] Kamil and Klinger report the response of their patients to a timed-disintegration pentaerythritol tetranitrate capsule as excellent, with nitroglycerin requirements reduced as much as 85%.[3]

1. Biegeleisen, H. I.: Clin. Med. 2:1005, 1955. 2. Roberts, J. T.: Clin. Med. 4:1375, 1957. 3. Kamil, M., and Klinger, I.: New York State J. Med. 59:3398, 1959.

PENTRITOL

Each Pentritol Tempule is a controlled disintegration capsule containing 30 mg. of pentaerythritol tetranitrate in granular form. An initial dose of 10 mg. is released at once; a second dose 4 hours later; and a third dose 8 hours after ingestion. Thus, each Tempule affords at least 12 hours of coronary vasodilation. ACTION AND USES: Effective therapy for and prophylaxis against anginal attacks. One Tempule morning and evening will provide 24 hours of effective medication, with a smooth, sustained clinical effect that has shown superior results. Pentritol reduces or eliminates nitroglycerin requirements, stops or reduces frequency of anginal attacks, eliminates or mitigates pain, and increases capacity for physical activity. CONTRAINDICATIONS: Observe caution in glaucoma. DOSAGE: One Pentritol Tempule morning and evening, approximately 12 hours apart. SUPPLIED: Bottles of 60 and 250. Also available: Pentritol®-B Tempules®, with 30 mg. pentaerythritol tetranitrate and 50 mg. butabarbital, for 12 hours of coronary vasodilation plus sedation.

ARMOUR PHARMACEUTICAL COMPANY
KANKAKEE, ILLINOIS • *Armour Means Protection*

© Jan. 1961, A. P. Co.

UNIVERSITY OF MICHIGAN LIBRARIES

with fresh myocardial infarctions who were seen at Hadassah University Hospital, Jerusalem. Twenty-four hours after 200 μc of I^{131} was administered orally to these patients, a scintillation counter registered more counts over the left side of the chest than over the right side. This increased left-to-right ratio was still apparent six to seven days following the ingestion of radioiodine. These effects were not seen in seven normal control patients.

The authors have followed up their preliminary findings with a study of 23 patients with fresh myocardial infarcts reported in the *American Journal of Cardiology*. In some cases, the increase in the number of counts over the left side of the chest was only minimal, but it consistently appeared 24 hours after the ingestion of radioiodine and remained for a period extending up to seven days.

In experiments performed on 21 control patients, a slightly increased left-to-right ratio occurred occasionally, but the effect was temporary. The authors have concluded from their investigation that the oral administration of radioiodine may have practical applications in the diagnosis of myocardial infarction.

Peptic ulcer in children—In *Dapim Refuiim*, A. Ehrlich, Central Emek Hospital, Affula, has described six cases of peptic ulcer in children whose ages ranged from 7 to 13 years. In all six patients, the predominant symptom was abdominal pain; this was accompanied by vomiting in four patients. Two patients had a gastric ulcer, one had a prepyloric ulcer, and three had a duodenal ulcer. Conservative treatment produced excellent results in most of these patients. However, a duodenal ulcer in a 13 year old boy in this series of patients was treated by subtotal gastrectomy 10 years after the diagnosis of ulcer was originally established.

Peptic ulcer probably occurs more commonly in children than is generally thought, but it is diagnosed infrequently because of the difficulty in eliciting the typical history of ulcer pains from children. In addition, even when peptic ulcer is suspected, it may be difficult to perform x-ray examinations and tests of gastric juice in very young patients. Generally, peptic ulcer is diagnosed only when some serious complication appears, such as perforation or gastrointestinal hemorrhage. It is possible that the incidence of such complications would be reduced if peptic ulcer could be diagnosed earlier and appropriate treatment given.

JAPAN

Brain hydrolysates in treatment of mental deficiency—Since 1954, when Harrer and co-workers introduced the use of brain hydrolysates in the treatment of mental deficiency, this therapy has been applied clinically in Japan. Dr. Tokijiro Sato and associates, Tohoku University Medical Faculty, Sendai, have reported their observations on the use of brain hydrolysates in 14 mentally deficient children in the *Japanese Journal of Child Psychiatry*. There were seven boys and seven girls, all of whom were receiving educational treatment at a primary school. Results of tests of intelligence and social maturation in all patients were similar. For a period of one year, one-half of the patients (the control group) received a placebo, and the other half (the experimental group) were given brain hydrolysates. Both groups had intelligence tests, social maturation tests and electroencephalographic studies nine months after treatment was begun and nine months following its discontinuation. The results of a two year follow-up study are as follows.

1. A statistically significant elevation in the intelligence index, particularly in the verbal test, was noted for those patients receiving the brain hydrolysates.

2. The results of the social maturation test showed yearly improvement in both groups, which probably resulted from the educational treatment rather than from administration of the brain hydrolysates.

3. The electroencephalographic findings showed improvement for the majority of the experimental group but not for the control group. However, this improvement occurred primarily in the regulation of the basic rhythm and not in the abnormal discharges, which are not easily corrected.

4. From the psychopathologic viewpoint, no clear-cut improvement was noted in intelligence, behavior problems or emotional disorders in the children with borderline intelligence in both groups.

The authors found that administration of brain hydrolysates produced a favorable effect in morons and patients with mild imbecility who did

(Continued on page A-101)

Daricon®

IN BRIEF

DARICON is oxyphencyclimine hydrochloride, a long-acting, highly effective anticholinergic. DARICON provides 24-hour relief from the pain and discomfort associated with g.i. disturbances, usually on just b.i.d. dosage.

Indications: DARICON is valuable for the adjunctive management of peptic ulcers—duodenal, gastric and marginal types; functional bowel syndrome—irritable colon, spastic colon including mucous colitis; pylorospasm, cardiospasm; chronic, nonspecific ulcerative colitis; biliary tract disease, including cholecystitis and cholelithiasis; hiatus hernia accompanied by esophagitis or ulcer; gastritis, acute or hypertrophic; duodenitis; bladder spasm with or without cystitis; ureteral spasm, as with stones or pyelonephritis.

Side Effects and Precautions: Dryness of the mouth is the most common peripheral effect. Blurring of vision, constipation, and urinary hesitancy or retention occur infrequently. These effects may decrease or disappear as therapy continues, or can be minimized by adjustment of dosage. Care should be exercised in using DARICON in patients with prostatic hypertrophy, in whom urinary retention may occur. The use of DARICON as well as other anticholinergics in patients with an associated glaucoma is not recommended except with ophthalmological approval and supervision.

Administration and Dosage: The average adult dosage is 10 mg. of DARICON given twice daily—in the morning and at night before retiring. (Dosage should be adjusted in relation to therapeutic response.) As much as 50 mg. daily is acceptable to some adult patients. As little as 5 mg. daily is therapeutically effective in some adult patients.

Supplied: DARICON is supplied as a white, scored 10 mg. tablet.

More detailed professional information available on request.

not have any marked organic changes. This treatment had some effect on severe imbecility with marked organic changes, but there was little hope of improvement for such patients. In patients with severe imbecility but mild organic changes, brain hydrolysates produced desirable emotional changes; the authors suggested that a combination of brain hydrolysates and behavioral stabilization might effect an improvement in these patients which would allow them to benefit from education.

SPAIN

Eye disease—The Spanish National Ophthalmological Institute will soon be 100 years old. Approximately 40 new patients are seen daily at the Institute, although all of its 250 beds are seldom in use at any one time. The Institute is a part of the government's welfare program, and its services are free. The numerous medical students studying at the Institute intend to become eye specialists.

Dr. Juan Arjona Trapote, director of the Institute, stated that 412 eye operations were performed there over a period of two months. The most frequent operations are for cataract, which is usually not considered dangerous unless it is congenital. Other more difficult and laborious operations also have been performed, including those for detachment of the retina, intraocular tumors, etc.

Today there are fewer blind people in Spain than ever before because trachoma has practically disappeared. A few years ago trachomatous infection almost invariably led to total blindness, but the discovery of the virus *Chlamydozoon trachomatosis* and the use of TERRAMYCIN® have reduced the incidence of this disease by 40 per cent. Only occasional cases are now seen.

When asked if patients with serious eye diseases have to go abroad for the best ophthalmologic care, Dr. Arjona replied that Spain has many excellent ophthalmologists and many of the newest and best ophthalmologic treatments and operative procedures are of Spanish origin. He also stated that some conditions, such as those caused by syphilis, glycosuria, poor hygiene, etc., have been almost totally eradicated.

UNIVERSITY OF MICHIGAN LIBRARIES

Psoriasis of 37 yrs' duration. Previous therapy produced no improvements.

Same Patient: Clearing after 2 mos' treatment with Lipan. Dosage: 5 capsules 3 times daily.

ACHIEVE FREEDOM FROM PSORIASIS w/LIPAN

Over and over again, studies have shown Lipan Improved Capsules to be orally effective therapy. Lipan will, in most cases, give a rapid clinical response. Maintenance dosage frequently keeps the patient symptom-free.

Again, in a recent study[1] on psoriatics of long standing, 37.71% showed complete remission of symptoms, 32.26% showed decided improvement, and 12.90% showed moderate or temporary improvement.

These new studies on the use of Lipan Improved Capsules have demonstrated that the clinical results are in direct proportion to adequate daily dosage.[2,3]

Effectiveness of Lipan therapy increases as dosage is increased.

Dosage: For complete *Lipanization* (saturation dosage): 2 to 4 capsules before each meal: 1 to 2 capsules before between-meal snacks.

Each Lipan Improved Capsule contains: Pancreatin – 2000 mg., Pyridoxine HCl – 3 mg.

Reprints, Samples and Literature upon request

Spirt & Co., Inc.

Waterbury, Conn.

PDR
PAGE 747

REFERENCES: 1. Schwartzschild, L.: Oral Management of Psoriasis with a Lipotropic Agent. Clin. Med., Vol. 8, No. 4, (April) 1961.
2. Combes, F. C.: Management of Psoriasis as a Metabolic Lipid Disturbance. N. Y. St. Jrl. Med., Vol. 54, No. 13, July 1, 1954.
3. Rosenthal, T.: Management of Psoriasis. Clin. Med., Vol. 7, No. 3, (March) 1960.

An Obstetric-Gynecologic Survey of the Problem of Perinatal Casualties

ROBERT E. L. NESBITT, JR.*

Albany Medical College of Union University, Albany, New York

Any physician who corrects a significant medical disorder in a female prior to or during her childbearing years and thereby improves her general health is practicing preventive medicine in obstetrics; he is also laying the groundwork for a continuum of care and supervision throughout the reproductive years that is a prerequisite to effective obstetric management. The general physician is the key figure in providing this care, and it is every physician's responsibility to take the lead in establishing an effective program which will combat perinatal deaths.

ROBERT E. L. NESBITT, JR.

THE period of human existence between the end of the nineteenth week of gestation and the end of the first month of life is of special interest because the mortality rate during this "perinatal" period has not declined to the same degree as has the mortality rate in other ages of life.[1] In addition, it is apparent that several significant neurologic sequelae have their origin in conditions related to the perinatal period. It seems justified at present to assume that the same factors are prominent in both lethal and sublethal cases and that the arbitrary groupings of fetal mortality (early or late), premature birth, congenital anomalies, neonatal mortality and morbidity, and the aftermath of sublethal injuries of the brain represent for the most part merely the broad spectrum of the worst and the least of the gamut of related problems of reproduction.

Perinatal casualties apparently are not randomized throughout the general population. Rather, minority segments of the female population contribute the majority of the reproductive losses, and the disproportionate perinatal wastage among these women often is complicated by a deleterious factor that recurs or persists through successive pregnancies.

*Department of Obstetrics and Gynecology, Albany Medical College of Union University, Albany, New York.

Presented before the forty-fifth annual Assembly of the Interstate Postgraduate Medical Association at Pittsburgh.

Basic Approach to Improvement of Perinatal Salvage

The basic premise of the modern obstetric approach to perinatal salvage is that the fetus is a victim not only of its genetic constitution but also of its uterine environment and that, in most instances, if this environment is altered favorably either before conception or during pregnancy an improvement in perinatal salvage will be the inevitable dividend. This is the consensus of current obstetric opinion, and it is on this fundamental concept that most prophylactic and therapeutic approaches are based.

According to this expanded view of clinical responsibility, any practicing physician who corrects a significant medical disorder in a female prior to or during her childbearing years, and who thereby improves her general health, is participating in "preventive medicine" in obstetrics. Moreover, in providing such therapy for a potential mother he is laying the groundwork that is a prerequisite to effective obstetric care, namely, a continuum of care and supervision, preconceptional work-up and therapy, and painstaking execution of prophylactic examinations throughout the reproductive years. This program of periodic screening includes a survey of the general medical status, evaluation of emotional factors, assessment of nutrition, and careful evaluation of the gynecologic history, together with complete physical examinations and special tests as indicated. The general physician is the key figure in providing this care, and he must bear the heavy burden of responsibility of knowing that a continuum of care will influence appreciably the reproductive efficiency of his patients. This prophylactic approach to the problems of reproduction may have far greater influence in assuring successful gestation than energetic treatment by a specialist during pregnancy after signs or symptoms of a pathologic condition have appeared.

Factors Related to Disproportionate Perinatal Wastage

Multiple clinical factors must be weighed and summed up in assessing the problems of reproductive wastage. As our knowledge increases, it is becoming more apparent that only a minority of obstetric patients are free of all conditions or alterations which are known to decrease to some extent the "optimal" perinatal salvage rates. In attempting to delineate areas of special concern, the following interrelated factors seem to be important as common denominators in patients who evidence disproportionate perinatal wastage:

- Advanced maternal age.
- Obstetric history of abortion or perinatal mortality and morbidity.
- Lower socioeconomic groups (poor diet).
- Prolonged conception-effort time.
- Maternal diseases such as hypertensive cardiovascular disease, diabetes, heart disease and tuberculosis.
- Endocrine imbalance (inadequate uterine preparation).
- Pelvic disease (uterine myomas, endometriosis, ovarian tumors).
- Anatomic defects of generative tract (uterine anomalies, incompetent cervix).
- Blood incompatibilities between mother and fetus (Rh, ABO).
- Neglected or inadequate preconceptional work-up and therapy.
- Absent or inadequate prenatal supervision.

Clinicians who routinely evaluate their patients carefully will be likely to uncover the factors inimical to fetal welfare and will be able to identify priority-risk groups who warrant special care and treatment. Thus, all patients should be subjected to critical review in an effort to identify those who may contribute most heavily to reproductive wastage.

Screening Technic to Detect Endocrine Disturbances

An effort should be made also to screen presumably "normal" obstetric patients for evidence of early, reversible endocrine disturbances before clinical signs and symptoms indicate that the pregnancy is threatened. For this purpose the vaginal smear for cytohormonal study[2] should be an integral part of the physician's armamentarium. It is a practical screening technic for determining the end effect of the combined action of estrogens and

progesterone. Moreover, it is a highly accurate method for forecasting the outcome of pregnancy and for testing the efficacy of a therapeutic regimen.

The relationship of the endometrium (decidua) and formation of the chorion is crucial in determining the type of placenta that will be developed. Subnormal size or gross deformation of the placenta, or complications resulting from its location or attachment, as well as abortion and premature birth may be due to faulty placentation and impaired intrauterine environment. If the vaginal smear is abnormal, the likelihood of abortion or premature labor is related directly to the percentage of karyopyknotic cells in the colpocytogram.

This screening technic may be supplemented by more specialized and refined methods of exploring crucial facets of reproductive physiology in selected cases. Patients who have a reversible progestational defect, as reflected by a change in the smear in response to hormonal therapy, usually have a normal titer of chorionic gonadotropins. When the titer is low, the outlook for the pregnancy is grave, regardless of cytologic findings. Thus, in the poor-risk groups, weekly vaginal smears during the critical months of early pregnancy provide an effective method of testing the efficacy of the therapeutic regimen and the wisdom of continuing it. In my experience, the empiric use of hormonal therapy, once signs of threatened abortion or premature labor have appeared, is of limited value.

Patients who have required thyroid therapy prior to conception should be treated more intensively during the early months of pregnancy if the protein-bound iodine level does not rise above the normal value for the nonpregnant state.

Premature Birth

The relationship between the infant's birth weight and perinatal deaths is one of the most pronounced associations observed in any assessment of reproductive wastage. About two-thirds of all perinatal deaths occur among fetuses or infants weighing less than 2500 gm. at birth. Uterine irritability is commonly associated with toxemia, certain maternal infections, hydramnios, fetal malpresentation and multiple gestation; thus, adequate rest in bed, which reduces uterine tone and improves the flow of blood in that organ, is a desirable prophylactic measure in conjunction with more specific therapy.

Unnerus[3] recently called attention to the relationship of the heart volume of the mother, the birth weight of the infant, and the incidence of prematurity. The percentage risk of premature delivery decreased by 50 per cent for every increase of 100 cc. in the heart volume. In about two-thirds of the pregnancies resulting in premature delivery, the heart volume of the mother was less than 600 cc. In the pregnancies resulting in full-term delivery, only one-third of the mothers had a heart volume of less than 600 cc. A regimen of supervised rest in bed for the group of women who had a reduced heart volume resulted in a significant reduction in the incidence of premature birth.

Careful prenatal supervision of certain medical diseases complicating pregnancy, such as chronic hypertension, cardiac disease and diabetes (including several periods of hospitalization during pregnancy for evaluation, rest and control), will prevent premature labor in many cases. This meticulous prenatal care also minimizes the risk of toxemia and placental abruption, which are common causes of premature labor or therapeutic intervention at an early date. Special attention should be directed to detection and eradication of bacterial infections, particularly in the urinary tract. Evidence has been presented recently which indicates that hormonal changes accompanying pregnancy act as predisposing factors in increasing the incidence of bacteriuria during pregnancy and in sensitizing the uterus to endotoxins.[4]

Diet, Hygiene and Excessive Smoking

In addition to specific and supportive therapy for acute and chronic illness, evidence has accrued which emphasizes the importance of good diet and hygiene and calls attention to other factors such as excessive smoking. Positive correlations are found between inadequate diet and certain obstetric and fetal

UNIVERSITY OF MICHIGAN LIBRARIES

complications. A good diet is an important feature of preconceptional medical care and a requirement of effective antepartum care.

Simpson[5] has shown that excessive smoking during pregnancy retards fetal growth. This reduction in birth weight seems to be unrelated to maternal weight, age or parity or to complications of pregnancy. It has been hypothesized that the effect of tobacco smoke may be the effect of nicotine in causing peripheral vasoconstriction and restriction of placental circulation. Carbon monoxide in the blood of mother and fetus as a result of smoking may also be a deleterious factor in certain hypoxic conditions of pregnancy.[6]

Surgical Correction of Diseases and Anomalies

In certain cases of pelvic disease or uterine anomalies, an improved prognosis may be offered by corrective or plastic procedures, particularly surgical repair of uterus bicornis or uterus septus or removal of uterine or adnexal tumors. In carefully selected cases, performance of the Shirodkar operation, which is designed to close an incompetent cervical os, at about the eighteenth gestational week holds some promise in preventing late abortion and premature labor. When incompetence of the cervix is suspected, weekly examinations of the cervix are made after the twelfth week. Characteristically the cervix undergoes progressive effacement and dilatation without evidence of uterine hypertonia. The internal cervical os dilates, the membranes bulge through the aperture, and, if the course of events is unaltered by surgical intervention, the membranes rupture spontaneously and labor ensues. Careful work-up to exclude other etiologic factors should be carried out preconceptionally, and before surgical correction is instituted it has been our policy to document the presence of normal uterine tone and a progesterone-dominated vaginal smear.

Additional Principles of Management

Several other principles of management favor the prolongation of intrauterine existence in selected cases, without imposing appreciable risks on the mother.

1. Patients who have normal uterine tone, minimal vaginal bleeding and a normal fetal heart rate may be managed expectantly in the hospital, provided blood is held in readiness, facilities for immediate delivery by either the vaginal or the abdominal route are available, and constant supervision is possible. About one-third of patients with placenta previa can be managed in this way with a view to delaying definitive examination and delivery until the fetus has achieved greater maturity. In about two-thirds of the patients, however, an intracervical digital examination under "double setup" precautions is required to establish the diagnosis and decide on a definitive method of delivery, because the fetus is of full-term size, labor has begun, or the amount of bleeding is alarming. Also, when the patient has persistent abdominal pain or when the resting tone of the uterus is increased, it is mandatory to establish the diagnosis. In the majority of these cases placental abruption will have occurred and the outlook for mother and fetus will depend on the promptness of delivery and adequate replacement of blood. In general, fetal prognosis depends on the maturity of the fetus, the severity of placental abruption, the presence or absence of associated toxemia and its severity, and the number of hours necessary to accomplish delivery. Timely intervention in partial abruption of the placenta, by the most conservative procedure possible (which may mean abdominal delivery in about one-fourth of the cases), may prevent fetal death from anoxia.

2. Expectant treatment of a patient with premature rupture of the membranes may be preferable to induction of labor when the fetus is immature. Perinatal mortality is not increased provided the uterus is noncontractile. The patient should be kept in the hospital until labor ensues unless the drainage of fluid ceases. Chemotherapy is not indicated during this latent period unless there is evidence of uterine contractility.

3. An attempt should be made to confirm maturity of the fetus before induction of labor or performance of cesarean section to help avoid the hazards of delivery of an immature infant.

Conduct of Premature Labor and Delivery

Premature labor and delivery should be conducted under one of the technics of conduction anesthesia, principally pudendal block or continuous caudal anesthesia. Meticulous care must be taken to avoid fetal narcosis, so that the immature respiratory center will not be depressed and pre-existing hypoxic effects will not be compounded. By the same token, one should employ artificial uterine stimulation and other technics capable of reducing fetal oxygenation sparingly and avoid them altogether when uterine contractions are incoordinated.

It is routine procedure in our institution to administer oxygen to the mother for about 15 minutes prior to delivery in an effort to increase the oxygen content and saturation of the cord blood. The infant should be delivered by the simplest method possible to avoid intracranial injury. Usually it is preferable to deliver the infant spontaneously over a generous episiotomy; or gentle traction with forceps may be necessary. Prolonged cranial pressure from arrested progress in the second stage of labor should be averted. It is equally important to avoid the cranial stress of a precipitous and uncontrolled delivery.

After delivery, the infant is kept at the level of the placenta or below it, and clamping of the cord is deferred until pulsations cease. The immediate considerations are establishment of a clear airway, avoidance of trauma and chilling, and maintenance of proper oxygenation, temperature, humidity and fluid-electrolyte balance. Antibiotics may be administered to immature infants to minimize the hazards of infection, particularly if labor has been complicated or if the infant has respiratory difficulty. Use of 15 per cent oxygen or a lowered environmental temperature in the postnatal period needs further study before it can be employed generally in the management of the newborn infant.[7]

Selection of Method of Delivery

The highest possible standards of obstetric and pediatric care have been necessary to maintain the survival rates we now have. This presupposes continued emphasis on a clinical attitude that stresses conservative technics of management as a means of avoiding fetal anoxia and trauma. It depends on an appreciation of the classical art of obstetrics, on knowing when and how to intervene and when it is best to support the patient without active intervention. It implies proper evaluation of the pelvis, judicious use of oxytocic stimulation, and correct use of abdominal delivery instead of internal version, difficult extraction and application of forceps on the unengaged head. The very real possibility of sublethal or even lethal injury of the brain has had direct bearing on the wisdom of the performance of cesarean section in certain cases. It should be selected as a proper and timely method of definitive management, not as a last resort after all other methods fail or after the fetus has suffered irreversible injury.

To achieve optimal perinatal salvage, a cesarean section rate above the mean would seem to be necessary in the management of elderly primigravidas. Likewise, the abdominal route of delivery is preferable in many cases of pelvic contraction, fetal malpresentation, and inert labor of the dyskinetic type that fails to respond to rest, hydration and conservative supportive measures. Selection of a proper method of delivery in the best interests of the fetus often requires considerable experience and a nicety of judgment. The fact that anoxia and birth injury are still responsible for more perinatal deaths and permanent disabilities than any other factors, in spite of improvement in recent years, attests to the difficulty of this clinical assessment.

It is appropriate to emphasize that promiscuous abdominal intervention is fraught with nearly as much hazard as is entailed in depriving patients of the safeguard of this method of delivery when it is truly indicated. Cesarean section is frequently noted to be the mode of delivery of premature infants who die during the neonatal period as a result of pulmonary problems, particularly hyalinelike membrane and atelectasis. Moreover, at least half of the intracranial hemorrhages in premature infants occur in cases in which there

has not been actual obstetric intervention. In these cases the etiologic factor is anoxic vascular injury which has its origin in various complications of pregnancy and parturition that compromise the supply of oxygen to the fetal brain.[1] Even repeated cesarean sections performed electively under optimal conditions are associated with a perinatal mortality rate of more than 1 per cent.

Induction of Labor

The increasing use of uterine stimulation without proper safeguards as an adjunct in elective induction of labor or to hasten "slow" parturition should be regarded with considerable concern. There are risks to both the mother and the fetus when oxytocin is administered without strict indications and rigid safeguards. If oxytocin is administered when incoordinated uterine contractions are present, it may aggravate the dysfunction rather than correct it, and thus place the fetus in possible jeopardy from hypoxia. In our experience, relaxin has not been effective in hastening parturition, either given alone or in conjunction with oxytocin, and it does not lessen the potential risks of the latter agent.[8]

In properly selected cases the induction of labor is a very effective therapeutic approach to many obstetric problems. In certain patients in whom pregnancy is complicated by toxemia, hypertensive cardiovascular disease, placental abruption, marginal placenta previa, diabetes, or Rh sensitization, induction of labor may offer the best chance for fetal survival. In the event of Rh sensitization it is desirable to induce labor at about the thirty-eighth week of gestation when the patient has a progressive or sudden rise in antibody titer, when a significant albumin or serum antibody titer exists throughout most of the pregnancy, when there is a history of the birth of an erythroblastotic infant, and when there is reasonable likelihood that the husband is homozygous-positive.

Every effort should be exerted to prevent or minimize fetal anoxia and trauma in the conduct of labor and delivery. The pediatrician should be on hand to accept the baby at birth, and the necessary equipment should be available for resuscitation and immediate exchange transfusion. Kernicterus is a particular problem of the prematurely born infant, but this hazard can be minimized by exchange transfusions given early and repeated as necessary.

Termination of pregnancy several weeks before term is desirable when there is a likelihood that placental function is being jeopardized and there is risk of fetal death in utero. Certain hypertensive, toxemic and diabetic patients fall into this category. It has been our policy not to intercede in cases of postdatism unless other specific complications arise that are inimical to fetal welfare, such as hypertensive disease and toxemia. The hazards to the fetus in protracted gestation prior to the onset of labor are insufficient to outweigh the dangers of routine and often drastic measures to keep pregnancies from becoming "postdate." Early recognition and treatment of complications, which usually take the form of placental dysfunction, prolonged labor, and inertia, will enable the obstetrician to minimize the factors that tend to compound hypoxic effects in the fetus.[9] A small minority of infants, particularly those subjected to inanition and hypoxia, presumably as a result of placental dysfunction, in the last days or weeks of pregnancy or, more commonly, during labor, may present problems of intracranial injury or respiratory distress. The great majority of the infants of "postdate" mothers will not require special care.

Infection as a Cause of Neonatal Death

Infection as a cause of neonatal death deserves special comment, since it is found terminally in many infants dying of other conditions. Deaths that are properly classified as caused by infection should be reported as deaths due to infection as the underlying cause, not merely as an ultimate complication. Pneumonia or septicemia within the first few days of life is usually acquired in utero. Long labor, prolonged rupture of the membranes, particularly when the fetus is of full-term size, and intrapartum fevers are often associated with contamination of the amniotic

aid by pathogenic bacteria. In many cases infection in the newborn infant is unheralded by objective signs or symptoms of sepsis in the mother. This is particularly true of infants born prematurely, in whom progressive and widespread infection may develop without prior warning signs. In many instances, there will be evidence in the mother of inflammation in the cord or placenta, and this evidence may be used as the basis for early institution of chemotherapy in the newborn infant. In spite of intensive treatment of the mother or infant, or both, however, infection remains a significant neonatal hazard. The most common infections acquired after birth are staphylococcal, but in the majority of cases these are manifested clinically after the infant has been taken home from the hospital.

Prevention of Fetal Malformation

At present, prophylaxis and therapy can influence malformation only slightly, although it is possible that more effective preconceptional care and improvement of the hormonal milieu and uterine environment will reduce the likelihood of fetal maldevelopment in selected cases. At the present time, severe malformation accounts for about 10 per cent of all perinatal deaths.

There would seem to be at least two additional approaches to the prevention of perinatal casualties due to fetal malformation. First, it may be possible to lower the incidence of deformity in subsequent generations by minimizing exposure of maternal and fetal gonads to irradiation. The clinician should curtail the use of irradiation to the lowest limits compatible with safe management of pregnancy, labor and delivery. Second, the likelihood that an anomaly exists which is amenable to surgical correction should be borne in mind constantly. Expert diagnosis and treatment may increase to some extent the over-all salvage in this group.

An Effective Program to Combat Perinatal Death

The sharp decline in perinatal mortality rates observed during the years from 1935 to 1945, a period of rapid medical and social progress, has, unfortunately, leveled off gradually during the past decade. It is apparent, however, that the millennium has not been reached; nor does it appear to be near at hand. Based on the criticisms of perinatal-mortality conferences and the assessments of special groups studying this problem, in as many as one-fourth of the cases in which perinatal death occurs the death is "preventable" or the care of the mother is deficient or objectionable in one way or another when compared with the ideal. Thus, it would not seem to be needless repetition to reiterate the general principles of sound obstetric care and responsibility. In addition, it would seem pertinent to emphasize the following medical and social steps in developing an effective program to combat perinatal death:[10]

1. Adoption of a multidisciplinary approach to the problem.
2. Wider application of what is known about obstetric and pediatric care.
3. Elevation of living standards and resources.
4. Expansion of facilities designed for antepartum care.
5. Expansion of both professional and lay education.
6. Emphasis on preconceptional care and expansion of facilities to support this program.
7. Continuous analysis of perinatal mortality and morbidity at the national and local levels.
8. Expansion of research monies, facilities and effort.
9. Development of an attitude that views obstetrics from the standpoint of the fetus and provides a continuum of integrated care for the infant throughout all phases of his biologic development.
10. Expansion of facilities for the prospective study, follow-up and care of infants who have been subjected to some degree of insult during the perinatal period.

An attack on the problem of perinatal wastage must be part of the general health program and cannot be relegated exclusively to any single group of medical workers. The problem is primarily one which concerns

everyone interested in maternal and child health, and this means the entire community. Perinatal loss is one of the most sensitive indexes of the social and economic level of a community. The impact of this problem transcends every stratum of our society and has broad implications that concern each of us. It falls to the lot of every physician as a medical man and as a citizen to take the lead in assuming responsibility for establishing an effective program to combat these tragic losses.

REFERENCES

1. Nesbitt, R. E. L., Jr.: Perinatal Loss in Modern Obstetrics. Philadelphia, F. A. Davis Company, 1957.
2. Nesbitt, R. E. L., Jr., Garcia, R. and Rome, D. S.: The prognostic value of vaginal cytology in pregnancy. Obst. & Gynec. 17:2-8 (January) 1961.
3. Unnerus, C. E.: Heart volume and prematurity. Acta obst. et gynec. scandinav. 38:340, 1959.
4. Kass, E. H.: Hormones and host resistance to infection. Bact. Rev. 24:180-185 (March) 1960.
5. Simpson, W. J.: A preliminary report on cigarette smoking and the incidence of prematurity. Am. J. Obst. & Gynec. 73:808-815 (April) 1957.
6. Haddon, W., Jr., Nesbitt, R. E. L., Jr., Garcia, R. and Wendel, W. O.: Smoking in obstetrics: I. Carbon monoxide in blood during gestation and at term. Obst. & Gynec. (In press.)
7. Karlberg, P.: Physiological aspects of temperature and oxygen effects on newborn infants. Proceedings of the Ninth Congress of Paediatrics, Montreal, Canada, July 1959, pp. 29-38.
8. Nesbitt, R. E. L., Jr. and Cirigliano, G.: Use of relaxin during parturition; clinical observations. New York J. Med. 61:90-97 (January 1) 1961.
9. Nesbitt, R. E. L., Jr.: Postmature pregnancy: A clinical and pathologic appraisal. Obst. & Gynec. 8:157 (August) 1956.
10. ——: Perinatal mortality after the period of fetal viability. New York J. Med. (In press.)

Postgraduate Clinical NOTES

156. CANCER OF FEMALE GENITALIA

Although many advances have been made in the treatment of malignant lesions of the female genitalia, surgery and radiation remain the only methods that can "cure" the disease. These methods are being applied with better results in long-term survival and in comfort of the patient, the latter being an important but less often emphasized part of the physician's role. In some human cancers there is much discussion these days about whether earlier treatment is a significant factor in the over-all result of therapy. In cancers of the vulva, cervix, body of the uterus, and ovaries, the stage of the disease at the time of treatment correlates strikingly with the ultimate salvage regardless of the method of therapy. The local extent is, in fact, more important in prognosis than the microscopical grading of the tumor. The steadily rising long-term survivals are directly related to the increased proportion of cases diagnosed in earlier stages of the disease and to newer diagnostic methods, and education of both the physician and the patient is important in this regard.

R. R. Curtin and H. Ulfelder, Gynecology, *New England Journal of Medicine*, October 22, 1959, p. 849

Chronic Bronchitis and Pulmonary Emphysema

RICHARD V. EBERT*

University of Arkansas Medical Center, Little Rock

The impairment of respiratory function associated with chronic bronchitis and pulmonary emphysema is reviewed. Environmental factors play a role in pathogenesis of the condition. In diagnosis, the history is more helpful than are physical findings and radiologic changes. The most useful functional test is a measure of vital capacity together with an estimate of expiratory flow rate. Recommendations for management are made, stressing sympathetic understanding by the physician. Measures for treatment of episodes of acute pulmonary insufficiency also are discussed briefly.

RICHARD V. EBERT

To understand the clinical manifestations of bronchitis and pulmonary emphysema, one must have a knowledge of the anatomic and physiologic properties of the lungs. The respiratory system in the lungs can be considered as consisting of two parts (figure 1). The first part is composed of the trachea, bronchi and bronchioles. This system of tubes serves to conduct air to the terminal air spaces, which can be considered the second part. The trachea, bronchi and bronchioles contain only a small proportion of the total air in the lungs. The walls of the bronchi are lined by ciliated epithelium and contain numerous mucous glands. This mucus serves as a protective coating but if excessive in amount can readily obstruct the flow of air. The conducting pathways provide resistance to the movement of air into and out of the lungs.

The terminal air spaces include the respiratory bronchioles, alveolar ducts, atria and alveoli. Most of the air in the lungs is contained in these structures. Because of their small size, an enormous surface area is available for the

*Professor and Head, Department of Medicine, University of Arkansas Medical Center, Little Rock, Arkansas.

Presented before the forty-fifth annual Assembly of the Interstate Postgraduate Medical Association at Pittsburgh.

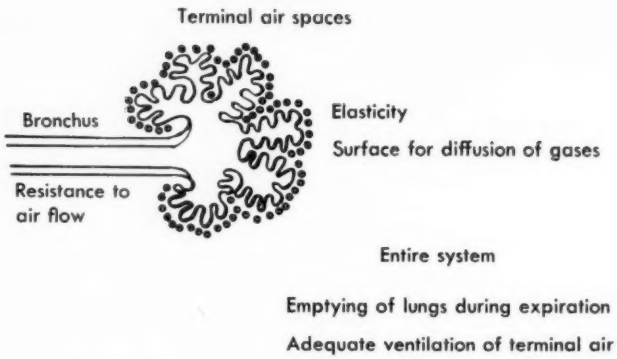


FIGURE 1. Respiratory function of the terminal air spaces in the lungs and of the trachea, bronchi and bronchioles.

diffusion of gases between the alveolar air and the pulmonary capillary blood. In man, this surface area has been estimated to be 25 square meters.

The elastic properties of the lung appear to be intimately related to the terminal air spaces. Part of the lung's elasticity is derived from the surface tension of the fluid surface of the alveoli, and part is derived from the properties of the walls of these structures. The elastic properties of the lung are dependent on the size of the terminal air spaces and are altered significantly when the air spaces are enlarged, as in emphysema.

Normal movement of air into and out of the lungs is dependent on the presence of normal dimensions of all these structures. The rate of movement of air out of the lungs during expiration is a function of their elasticity and the resistance to the flow of air in the tracheobronchial tree. It is a curious fact that air cannot be forced from the lung by external compression; the bronchioles and small bronchi will collapse if they are exposed to external pressure.

Effect of Bronchitis and Pulmonary Emphysema on Pulmonary Function

With the foregoing remarks in mind, the impairment of pulmonary function associated with chronic bronchitis and pulmonary emphysema can be explained readily (table 1). The enlargement of the terminal air spaces alters the elasticity of the lung. Because the lungs empty inadequately, residual volume increases and vital capacity diminishes. The altered elasticity of the lung together with obstruction of the bronchi reduce the rate of expiratory air flow to a pronounced degree. As the pathologic process is localized rather than diffuse, some areas of the lung are ventilated better than others and air is distributed unequally to various parts of the lung. The replacement of normal alveoli by large air spaces reduces significantly the surface area available for diffusion.

Thus, bronchitis and emphysema together serve to alter the function of the lungs. In some instances, bronchitis with increased resistance to air flow is dominant; in others, the important factor is alteration of the terminal air spaces.

Pathologic Process

Much has been learned recently about the pathogenesis of bronchitis and emphysema. British workers have been particularly interested in the pathologic process involved in chronic bronchitis. Reid[1] has demonstrated that in addition to inflammatory changes in the walls of the bronchi and bronchioles, hypertrophy of the mucous glands and goblet cells often is observed. The latter change undoubtedly is related to the excessive production of mucoid sputum.

The pathologic picture of pulmonary emphysema is extremely varied.[2] In the advanced stage of the disease the normal structure of portions of the lung may be completely replaced by large air spaces of various size containing strands of tissue that represent remnants of the normal lung and blood vessels.

TABLE 1

EFFECT OF BRONCHITIS AND EMPHYSEMA

1. Change in pulmonary compartments Decrease in vital capacity and increase in residual volume
2. Decrease in rate of expiratory air flow
3. Unequal distribution of gases to various parts of the lung
4. Diminution of surface available for exchange of gases

TABLE 2

FACTORS INFLUENCING MORTALITY FROM BRONCHITIS AND EMPHYSEMA

Sex
Age
Urban or rural residence
Occupation
Atmospheric pollution
Cigarette smoking

It is interesting that even in the most severe forms of the disease there remain areas of relatively normal-appearing lung; these areas undoubtedly serve to sustain life. In certain instances of bronchitis and emphysema the lungs may contain large air spaces only in the center of the lobule, the so-called centrilobular emphysema.

An enlargement of the normal terminal air spaces is seen in the lungs of elderly persons, and emphysematous bullae may be found at necropsy in the lungs of aged persons who did not have respiratory symptoms during life. These changes undoubtedly are related to the increase in residual volume and the decrease in vital capacity associated with aging. Use of the term "senile emphysema" to describe the alterations in the lung associated with aging would appear to be a matter of individual preference.

Epidemiologic Studies

The exact cause of bronchitis and emphysema is unknown, but epidemiologic studies carried out in Great Britain[3] have cast considerable light on the origin of the diseases. Incidentally, British writers tend to use the term "chronic bronchitis" to encompass the whole syndrome, whereas Americans place more emphasis on "pulmonary emphysema." Chronic bronchitis is very common in Great Britain and is one of the major causes of death. Careful epidemiologic studies have shown clearly that environmental factors are important in its development (table 2). Deaths from this cause are more frequent among unskilled laborers than among office workers. The disease carries a higher mortality rate among residents of large urban areas than among persons living in rural districts. Both atmospheric pollution and cigarette smoking appear to play important roles in the disease. Finally, bronchitis and emphysema are much more common in men than in women and affect chiefly persons in the older age group.

Some Important Points in Diagnosis

The clinical manifestations and the diagnosis of bronchitis and pulmonary emphysema undoubtedly are familiar to all of you, and I shall attempt only to emphasize a few important points. The history is of immense value in diagnosis. Characteristically the patient complains of a long-standing chronic cough and of the insidious onset of exertional dyspnea. The degree of dyspnea increases until the patient is severely incapacitated. From time to time, attacks of acute bronchitis occur with an increase in cough and often with dyspnea at rest. The patient often refers to these attacks as asthma, but contrary to the asthmatic patient he is never symptom-free.

Physical examination and roentgenograms of the chest are of much less value in diagnosis. There has been much confusion in regard to the relationship of barrel chest and pulmonary emphysema. Suffice it to say that many elderly persons have barrel chest without any clinical or physiologic manifestations of emphysema.[4] In general, physical findings provide little aid in diagnosis, and the same can be said for roentgenograms of the chest. Except for large bullae, the lesions are not visible radiographically. Most of the roentgenologic findings are not specific for the disease. A roentgenogram of the chest is important, however, in a negative sense, in that it serves to exclude other diseases that may produce dyspnea, such as left ventricular failure and diffuse pulmonary fibrosis.

TABLE 3

TREATMENT OF CHRONIC BRONCHITIS AND PULMONARY EMPHYSEMA

Sympathetic understanding of the patient and the illness
Avoidance of smoking and atmospheric pollution
Antibiotic therapy
Bronchodilators, oral or aerosol
Cortisone and related steroids

TABLE 4

TREATMENT OF ACUTE PULMONARY INSUFFICIENCY

Avoid sedatives and narcotics
Antibiotic therapy
Use oxygen with caution
Bronchodilators and steroids
Mechanical respirators
Tracheostomy

The most useful function test is a measure of the vital capacity together with an estimate of the rate of expiratory air flow. While it is advantageous to have an objective measure of the rate of expiratory air flow, much information can be gained by visual inspection of the rate at which air is expelled while determining the vital capacity with a simple bellows-type spirometer. The McKesson-Scott spirometer* is simple, inexpensive and portable. Every physician should have an instrument for determining the vital capacity. Normally, a person can exhale 80 per cent of his vital capacity in one second. The expiratory air flow rate is greatly reduced in the presence of bronchitis and emphysema.

Treatment

As you know, results of treatment of bronchitis and emphysema often are discouraging. Of great importance to the patient is the knowledge that his physician has an interest in him and in his illness and is willing to work with him patiently over a long period (table 3). The discomfort produced by the dyspnea, the necessary restriction of activity, and the long course of the disease often lead to a sense of desperation on the part of the patient.

Avoidance of irritants or dust in the inspired air is essential. The chief of these irritants, of course, is tobacco smoke. Whatever the etiologic relation of smoking to bronchitis and emphysema (and this is not entirely clear), it is apparent that continuation of smoking is extremely harmful once the disease is established. Unfortunately, many of these patients are inveterate smokers and simply will not forego tobacco. If the patient refuses to stop smoking, a pipe is preferable to cigarettes, particularly if the smoke is not inhaled.

Antibiotics are, of course, necessary in management. Some controversy has arisen recently as to whether they should be used continuously or intermittently. Some evidence has been presented that the continuous use of tetracycline is valuable in reducing disability,[5,6] but usually this program is not practical because of the expense and because there is some danger of the development of resistant organisms or hypersensitivity to the drug. Most physicians prefer to use antibiotics for treatment of exacerbations of the bronchitis. I prefer penicillin in large doses given intramuscularly for two weeks or more. This course of therapy may give prolonged relief of symptoms. Other antibiotics may be valuable in individual cases.

Drugs which produce bronchodilatation are valuable in certain cases and relatively ineffective in others. Oral preparations containing ephedrine may be useful. Some patients obtain relief from the use of aerosols containing epinephrine or isoproterenol. The aerosol can be given in association with the use of intermittent positive-pressure breathing employing the Bennett machine.

The use of cortisone or related steroids is more controversial.[7] In my opinion they are not indicated in the majority of cases. The high incidence of complications associated with long-term steroid therapy precludes their use in most instances. Moreover, the steroids may not be significantly effective in many cases. An occasional patient will respond dramatically to steroid therapy, and such a patient may represent a case of true bronchial asthma that has been confused with bronchitis and emphysema.

*McKesson Appliance Company, Toledo, Ohio.

Other therapeutic measures have had varying degrees of success. The use of pneumoperitoneum is of questionable value and has been largely discarded. Breathing exercises may help certain patients, and possibly their beneficial effects are largely psychologic.

Management of Acute Pulmonary Insufficiency

Management of episodes of acute pulmonary insufficiency which accompany attacks of acute bronchitis deserves emphasis (table 4). An exacerbation of bronchitis produces further obstruction to air flow. Severe dyspnea ensues, and often the oxygen saturation of the arterial blood decreases and the carbon dioxide tension rises. Right-sided heart failure may occur as a result of hypoxia and pulmonary hypertension. Evidence of acute infection such as fever or leukocytosis may be absent. Nevertheless, the patient should receive prompt and effective therapy with antibiotics. These drugs often are lifesaving in these circumstances. Sedatives and narcotics should be avoided even though the patient is restless and disturbed. Depression of respiration may be lethal. Oxygen must be administered with great care, as it removes the hypoxic stimulus to ventilation through the chemoreceptors in the carotid and aortic bodies. Bronchodilators and cortisone may be helpful in individual cases. If the patient is severely ill and if hypoxia is pronounced and the carbon dioxide tension is increased, the use of a mechanical respirator may be lifesaving.[8,9] An intermittent positive-pressure respirator such as the Bennett machine can be used, with either a mask or an endotracheal tube. Sometimes secretions accumulate in the trachea and major bronchi because the patient is unable to cough, and in this situation tracheostomy should be performed. This permits adequate suction of tracheal and bronchial secretions. An anesthesiologist can be most helpful in the management of these desperately ill patients.

REFERENCES

1. Reid, L.: Chronic bronchitis and emphysema: A symposium. III. Pathological findings and radiological changes in chronic bronchitis and emphysema. (a) Pathological findings in chronic bronchitis. Brit. J. Radiol. 32:291-292 (May) 1959.
2. Leopold, J. G. and Gough, J.: The centrilobular form of hypertrophic emphysema and its relation to chronic bronchitis. Thorax 12:219-235 (September) 1957.
3. Fletcher, C. M.: Chronic bronchitis; its prevalence, nature and pathogenesis. Am. Rev. Respiratory Dis. 80:483-494 (October) 1959.
4. Pierce, J. A. and Ebert, R. V.: The barrel deformity of the chest, the senile lung and obstructive pulmonary emphysema. Am. J. Med. 25:13-22 (July) 1958.
5. Cherniak, N. S., Vosti, K. L., Dowling, H. F., Lepper, M. H. and Jackson, G. G.: Long term treatment of bronchiectasis and chronic bronchitis; a controlled study of the effects of tetracycline, penicillin, and an oleandomycin-penicillin mixture. A.M.A. Arch. Int. Med. 103:345-353 (March) 1959.
6. Francis, R. S. and Spacer, C. C.: Chemotherapy in chronic bronchitis; influence of daily penicillin and tetracycline on exacerbations and their cost: A report to the Research Committee of the British Tuberculosis Association by their Chronic Bronchitis Subcommittee. Brit. M. J. 1:297-303 (January 30) 1960.
7. Barach, A. L. and Pons, E. R., Jr.: Treatment of pulmonary emphysema and cor pulmonale with anti-inflammatory steroids. Ann. New York Acad. Sc. 82:963-971 (October 14) 1959.
8. Sieker, H. O. and Hickam, J. B.: Carbon dioxide intoxication: The clinical syndrome, its etiology and management with particular reference to the use of mechanical respirators. Medicine 35:389-423 (December) 1956.
9. Jameson, A. G., Ferrer, M. I. and Harvey, R. M.: Some effects of mechanical respirators upon respiratory gas exchange and ventilation in chronic pulmonary emphysema. Am. Rev. Respiratory Dis. 80:510-521 (October) 1959.

Analgesic Agents for the Relief of Acute Pain

MAX S. SADOVE AND M. J. SCHIFFRIN*

University of Illinois College of Medicine, Chicago

The management of acute pain remains a challenge, and search continues for an effective analgesic without addiction liability.

The authors report gratifying results achieved with the promising new analgesics alphaprodine hydrochloride, phenazocine, anileridine dihydrochloride, piminodine and an isoquinoline derivative.

Administration of tranquilizers in the overall management of pain allows use of smaller doses of narcotic analgesics. The authors have found that chlordiazepoxide effects remarkable changes in the fear factor associated with acute pain.

THE earliest practitioners of the medical sciences had the same goal as do our clinicians of today—to prevent or obtund human suffering and disease. While much progress has been made toward more successful management of acute pain, this problem still remains a challenge to all of us. Our purpose in this discussion is to sketch briefly what we are seeking, to explain how we study new analgesics, and to present summaries of our experience with the more promising new analgesics at the University of Illinois Research and Educational Hospitals.

All of us who are studying new analgesics have as our goal the development of an agent which more closely approximates the characteristics of the ideal analgesic (table 1). The primary target is to find an agent which can effectively relieve severe pain and which has no addiction liability. We have many agents which are useful in the management of severe pain, but they are narcotic analgesics; they produce tolerance and, eventually, the hideous spectacle of addiction. There is as yet no drug which obtunds severe visceral pain and is free of the hazard of addiction.

The search for the ideal agent has produced some useful new drugs. Some of these are shown in table 2, in which we have compared the properties of some of these newer analgesics with those of the older drugs. Alphaprodine hydrochloride (NISENTIL® hydrochloride) is a narcotic which produces an intense analgesic effect of short duration; thus,

*Division of Anesthesiology, University of Illinois College of Medicine, Chicago, Illinois.

Presented before the forty-fifth annual Assembly of the Interstate Postgraduate Medical Association at Pittsburgh.

MAX S. SADOVE

M. J. SCHIFFRIN

it has found a useful place as a supplement to nitrous oxide-oxygen anesthesia, as well as in short office and surgical procedures. Phenazocine (PRINADOL®) has a most interesting history, and we will describe some of our experiences with it later. It was hoped that this drug, in the usual analgesic dose, would have less addiction liability than drugs such as morphine. Although this hope was not realized completely, phenazocine has proved to be a very useful analgesic in many clinical problems of acute, severe pain; this is especially true when the clinical situation demands good sedation as well as analgesia. Anileridine dihydrochloride (LERITINE® dihydrochloride) is another of the new potent analgesics. This drug is effective by any route of administration and exerts an adequate sedative and an excellent hypnotic effect. Because of these characteristics, it is a good drug to give in the evening. It is also useful because its oral effectiveness allows it to be used occasionally when routine milder analgesics have failed because of the intensity of pain. We have found anileridine to be effective and safe throughout our clinical experience, which includes several hundreds of cases in which we have used it to supplement nitrous oxide-oxygen anesthesia.

Some of our studies[1-3] were carried out in the recovery room. Our usual procedure was to employ a double-blind technic and to use a placebo (saline) as well as a standard drug, meperidine hydrochloride (DEMEROL® hydrochloride). We feel that the reliability of the response to meperidine hydrochloride is such that any new drug must be compared with it. In our studies only those patients were included who had pain severe enough to justify the use of a narcotic analgesic. Records were kept of age, sex, weight, physical status, time, dosage and type of preoperative medications, the duration and type of surgery, anesthetic agents, other drugs used during surgery, etc. During the study period, pain, pulse rate, blood pressure, respiratory rate, respiratory minute volume, sedation, etc., were measured prior to the intramuscular injection of the narcotic and at 10, 20, 30, 60 and 120 minutes thereafter. The clinical evaluation was made by the same observer throughout the study.

In order to ensure that the observer was ignorant of the nature of the drugs, the order of their administration was changed frequently, and three or four different code numbers were assigned to each of the solutions. The observer knew that he was administering a narcotic analgesic or a control solution. He did not know if he was working with equivalent analgesic doses of different drugs or graded doses of a single drug at any one time. The recording and analysis of the data also were done by code in order to keep the recorder "blind." The codes were kept in a sealed, opaque envelope in the recovery room and were not broken until the study had been completed.

Piminodine (Alvodine) was one of the new narcotics which we used. We have found it to be a very potent and useful analgesic in the management of many pain problems. It produces very little respiratory depression, slight sedation, little side action, and adequate potency for severe pain; therefore, it is an excellent daytime narcotic analgesic. It has an ex-

TABLE 1

SOME PROPERTIES OF THE IDEAL ANALGESIC

1. No addiction liability
2. Freedom from tolerance
3. No respiratory depression
4. Oral effectiveness
5. More rapid onset of action
6. Appropriate intensity of analgesia
7. Controlled duration of effect
8. Specific effects on higher centers
9. Few undesirable reactions
10. Metabolism by nonhepatic enzymes
11. Availability of antidote
12. Low cost

TABLE 2

SOME CHARACTERISTICS OF NARCOTICS

GENERIC NAME	TRADE NAME	EQUIVALENT ANALGESIC DOSE (MG.)	MAXIMAL ANALGESIC INTENSITY	DURATION OF ANALGESIA	SEDATION	ROUTE OF ADMINISTRATION			
						Oral	*S.C.*	*I.M.*	*I.V.*
Morphine	Morphine	10	3	3	3	1	3	3	3
Codeine	Codeine	65?	1	2	1	2	3	3	
Dihydrocodeinone	HYCODAN®	10?	1	2	1	2	3		
Meperidine hydrochloride	DEMEROL® hydrochloride	100	3	2	2	2	3	3	3
Dihydromorphinone hydrochloride	DILAUDID® hydrochloride / HYMORPHAN®	2	3	2	3	2	3	3	
Metopon	Metopon	3	3	2	1	3			
Methadone	Methadone and others	10	3	3	2	3	3	3	
Alphaprodine hydrochloride	NISENTIL® hydrochloride	30	3	1	1		3	3	3
Levorphan tartrate	LEVO-DROMORAN® tartrate	2	3	3	2	3	3	3	3
Phenazocine	PRINADOL®	2	3	3	3			3	3
Anileridine dihydrochloride	LERITINE® dihydrochloride	25	3	3	3	3	3	3	3
Piminodine	Alvodine	15	3	3	<1	3	3	3	3

KEY: 1—Comparatively slight effect or duration.
2—Comparatively moderate effect or duration.
3—Comparatively marked effect or duration.

cellent safety factor and should be very useful for patients with terminal carcinoma.

We have made extensive studies of phenazocine.[4-6] This drug was synthesized at the National Institutes of Health by E. L. May. Dr. Nathan B. Eddy, to whom all of us are indebted for his many contributions, was instrumental in its development. The chemical relationship of morphine to phenazocine is shown in figure 1.

Throughout all our studies we have enjoyed the splendid and wholehearted cooperation of our colleagues in other departments of the college. The experience with phenazocine is an example of this type of cooperative venture. Drs. Branion and Kobak made possible the study of phenazocine for obstetric analgesia.[4] Two hundred and two patients in various stages of labor received intravenous doses of phenazocine, varying from 1.0 to 4.0 mg., for relief of pain. The average degree of analgesia was found to be statistically significant ($p = < 0.001$). The duration of analgesia following a single dose of phenazocine averaged 90 minutes. The average Apgar (modified) rating for the infants was 8.9. Delay in cry or respiration was observed in 22 of the 205 infants, but was definitely related to the administration of phenazocine in only seven (3.4 per cent). All depressed infants recovered uneventfully; there were no neonatal deaths. Side effects such as nausea, vomiting, hypotension and respiratory depression were not observed; 31 patients had pruritus of the face following the administration of phenazocine. Our over-all evaluation of phenazocine as an obstetric analgesic showed that it produced good or excellent response in 82 per cent of the patients in our series, and a poor or fair response in 18 per cent. The tranquillity and "contentedness" of the patients were really remarkable. It was as though a potent tranquilizer and analgesic had been used in large dosage. This drug deserves much greater use in this field.

With the valuable collaboration of Dr. Oscar Sugar we studied the usefulness of phenazocine as an analgesic for angiography of the cerebral vessels.[5] Ordinarily, angiography under local anesthesia is accompanied by a very

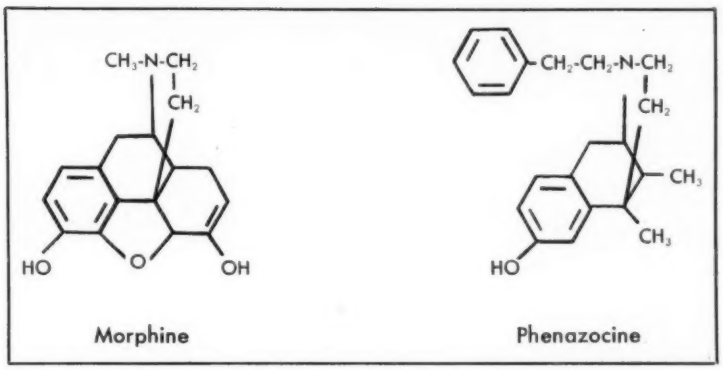


FIGURE 1. Chemical relationship of morphine to phenazocine.

uncomfortable sensation of heat, which may cause hypotension, nausea, vomiting or even unconsciousness. This is not so with the use of phenazocine. The blurring of x-ray pictures, due to even slight movement from this discomfort, is obviated. The patient can cooperate by assuming the necessary positions required by the x-ray technician. He also can move various parts of the body to demonstrate absence of complications.

The outstanding tribute to the method employing local anesthesia and phenazocine may be elicited from patients who have undergone angiography by other technics. Uniformly, the experience described is of a procedure scarcely remembered and not unpleasant, so that no serious objection to repetition has ever been voiced. This has been especially gratifying in those cases in which postoperative angiograms have been requested to visualize proper treatment of an aneurysm. The surgeons and anesthesiologists have been extremely happy with the safety, efficiency and dependability of phenazocine, and have reported on its use.

In our own area of anesthesiology, we have used phenazocine in 462 patients.[6] The drug was employed in different phases of anesthesia (e.g., induction, maintenance of anesthesia, and postoperative pain) and as an adjunct to local anesthesia. Its sedative and analgesic properties combined well with nitrous oxide and oxygen. Its action on the cardiovascular system seemed to be minimal, although it was depressant to respiration, which was easily remedied by levallorphan (LORFAN®). The doses of phenazocine varied from 2.0 to 6.0 mg. in increments of 0.2 to 1.0 mg. Postoperatively it provided pain relief for an average period of 90 minutes in doses of 1.5 mg. to 2.0 mg. intravenously or intramuscularly. A dose of more than 5 mg. caused respiratory depression, but this usually was not seen with 5 mg. or less. The respiratory depression becomes apparent if other drugs are used with phenazocine. PENTOTHAL® sodium is a frequent offender. Tranquilizers (phenothiazines) potentiate the undesirable side actions. When used alone, phenazocine is very benign and one of the finest drugs for a patient with chronic pain, especially if the patient may be expected to terminate the need for the narcotic. It may be easier to withdraw a patient from this narcotic than from most of the commonly used, potent narcotic agents.

Another type of analgesic has been gaining our increasing attention. This is an isoquinoline derivative, synthesized by Brossi and associates,[7] which appears to provide at least as much analgesia as does codeine, without the addiction liability of the narcotics. We were fortunate to be the first to publish clinical data on this compound.[8] The chemical structure of this analgesic, known by the experimental code designation Ro 4-1778/1, is shown in figure 2.

Encouraged by our preliminary clinical study, we undertook a full-scale, double-blind program comparing the oral administration of 50 doses each of placebo, 30 and 60 mg. codeine sulfate, 32 and 65 mg. dextro propoxyphene hydrochloride (DARVON®), and 30

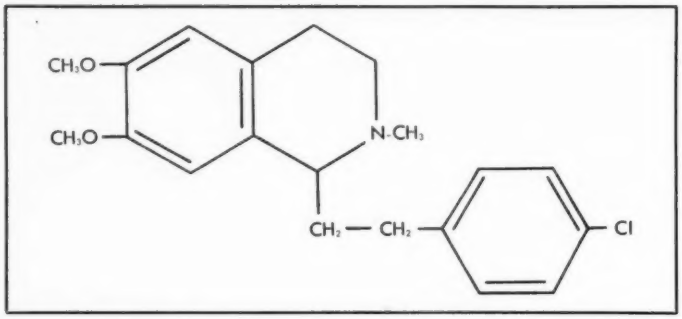


FIGURE 2. Structural formula of Ro 4-1778/1.

and 60 mg. Ro 4-1778/1. We selected a group of patients from the postsurgical orthopedic wards who were hospitalized for some time and had rather consistent requirements for orally administered analgesics of the potency of codeine. All these patients had the same general type of skeletal-muscular pain. Such uniformity is an advantage in testing different analgesic drugs and dosages. We are indebted to Dr. Robert D. Ray, professor and head of orthopedic surgery, whose cooperation made this study possible.

The results[9] of this program indicated that equal doses of codeine and Ro 4-1778/1 produced similar analgesia. The larger dose of dextro propoxyphene gave a response equal to 60 mg. of codeine or Ro 4-1778/1. Statistically, however, 32 mg. dextro propoxyphene was not significantly different from the placebo. We have enlarged our experience with Ro 4-1778/1 by using it in patients with chronic pain who cannot tolerate codeine. In all such cases gratifying results have been obtained without any undesirable side effects. In only one case, in which the drug was used intravenously, have we seen evidence of an increase in smooth muscle tone. Doses as large as 120 mg. have been given both intramuscularly and intravenously without any evidence of significant central nervous system depression. All our experience to date promises that this drug may be a useful and safe nonnarcotic analgesic.

It would not be proper for us to close this presentation without some statement relating to the importance of tranquilizers in the overall management of acute pain.[10] The phenothiazines are potent agents which enable us to use smaller doses of the narcotic analgesics. Our experience with chlorpromazine hydrochloride (THORAZINE® hydrochloride) and promethazine hydrochloride (PHENERGAN® hydrochloride) has been most rewarding, especially in the terminal cancer patient with severe pain. The combination of small doses of a narcotic and chlorpromazine and similar agents provides pain relief and sedation and lessens the hazards of continued use of large doses of narcotic analgesics. We confess a partiality for the use of promethazine and meperidine hydrochloride, especially in children. This is not simple bias. It is the result of our observations in several thousand cases. The combined use of small doses of these drugs makes these children comfortable. They are not drugged or oversedated; they seem to rest in a quiet sleep from which they are aroused easily. The dosage which we have found most useful is 0.5 mg. each of Phenergan and Demerol per pound of body weight given intramuscularly to a maximum of 50 mg. of each. In the event that respiratory or circulatory depression occurs, it is possible to obtund the narcotic effect and leave the residual tranquilizing effect by administering 0.5 mg. Lorfan intravenously.

In many instances, the main problem is the patient's reaction to pain rather than the intensity of pain. We keep at least two factors foremost in any consideration of a pain problem: (1) what the pain means to the patient and (2) to what extent fear and anxiety are contributing elements. The new agent chlordiazepoxide (LIBRIUM®) appears to be unique as an adjunct in the clinical management of the difficult severe pain problem. Chlordiaze-

p xide in a dosage of 5 to 10 mg. three times d ily obtunds inappropriate reactions to stress a d pain and gives the patient a sense of well-b ing without excessive sedation. It also has the advantage of being free of the troublesome s de effects that often accompany the use of the potent phenothiazines and the *Rauwolfia* derivatives. The marked alteration of the fear factor is so great that in many instances one is amazed by the results.

The management of pain should not be restricted to the use of analgesics and tranquilizers. It is important to recall that the best time to treat pain is before the pain occurs; hence, preventive measures should begin as early as possible. The finest "drug" at this time is TLC (tender loving care). Fundamental to this approach are tact, confidence, understanding, sympathy and patience. Specific drugs for the relief of nausea and vomiting and measures to promote wound healing are examples of useful concomitant therapy. Above all, if the physician tries to understand what the pain signifies to the patient, he will increase his opportunities for success in the management of pain.

REFERENCES

1. Sadove, M. S., Schiffrin, M. J., Nickerson, W. R. and Grove, W. J.: Use of meperidine and meperidine-levallorphan mixtures in the recovery room. J.A.M.A. 166:1432, 1958.
2. Sadove, M. S., Schiffrin, M. J. and Heller, R.: A clinical comparison of two narcotic analgesics. Current Therap. Res. 1:109, 1959.
3. Sadove, M. S., Sen, A. K. and Schiffrin, M. J.: Some new narcotic analgesics in the recovery room. Current Therap. Res. 2:61, 1960.
4. Sadove, M. S., Balagot, R. C., Branion, J. M. and Kobak, A. J.: A report of the use of a new agent, phenazocine, in obstetric analgesia. Obst. & Gynec. 16:448 (October) 1960.
5. Balagot, R. C., Sadove, M. S. and Sugar, O.: The use of phenazocine in cerebral angiography. J. Internat. Coll. Surgeons. (In press.)
6. Sadove, M. S. and Balagot, R. C.: Clinical appraisal of phenazocine—a new analgesic adjunct. (To be published.)
7. Brossi, A., Besendorf, H., Pellmont, B., Walter, M. and Schnider, O.: Halogensubstituierte 1-phenathyl-2-methyl-6, 7-dimethoxy-1,2,3,4-tetrahydroisochinoline als analgetica. Helvet. chim. acta. (In press.)
8. Sadove, M. S., Ali, S. M. and Schiffrin, M. J.: Preliminary clinical report on a new analgesic. Illinois M. J. 117:425, 1960.
9. Sadove, M. S., Schiffrin, M. J. and Ali, S. M.: A controlled clinical study of codeine, dextro propoxyphene and Ro 4-1778/1. Am. J. M. Sc. (In press.)
10. Sadove, M. S. and Schiffrin, M. J.: Tranquilizers in surgery. S. Clin. North America 39:231, 1959.

Postgraduate Clinical NOTES

157. BASIC RESEARCH

Basic research is the cutting of paths through the unknown. As most of us know today, it is the pacesetter for technology, and the raw material of invention. Its growth can be assisted, and its general value can be confidently asserted, but it depends, in the end, on the imaginative powers and scientific skills of the men who do it. Basic research is as hard as it is exciting, and while it contributes enormously to the national welfare, what usually moves the scientist is not so much this practical consequence of his labor as the simple but powerful urge to know how nature works. A free society can honor the scientist's curiosity without forgetting his social value.

Statement by the President's Science Advisory Committee, November 15, 1960

Advances in Electrocardiography

DONALD C. OVERY*

Great Falls, Montana

Three problems in electrocardiographic research which have been the subjects for investigations in the past 10 years are reviewed briefly.

1. A considerable portion of the inner wall of the left ventricle may be activated instantaneously, and only the outer layers of ventricular myocardium may contribute to formation of the QRS complex at the epicardial surface.

2. The sequence of intraventricular conduction has been shown to vary considerably, and there may be rather marked alterations in the order of ventricular excitation without clinical evidence of organic heart disease.

3. Electrocardiographic changes of ventricular hypertrophy are not always well correlated with clinical evidence of right or left ventricular enlargement.

DONALD C. OVERY

A HIGH light of the third decade of the twentieth century was the widespread application of the science of electrocardiography to clinical medicine. The demonstration that action potentials within atrial and ventricular musculature occurred in an orderly fashion and could be recorded rather simply and expediently led to wide acceptance of the electrocardiogram as a laboratory aid in the diagnosis of heart disease. Over the next 10 years knowledge concerning the differentiation of arrhythmias, the nature of the serial changes in myocardial infarction, and the changes seen with altered and delayed intraventricular conduction advanced rapidly.

Refinement in technics of recording electrocardiograms did much to further the application of this science in the physician's office and the hospital laboratory. Few physicians can still recall having a patient sit in a chair with his feet and arms in a brine solution while a very sensitive string galvanometer was standardized individually for each limb lead in order to record the cardiac potential. The direct-writing amplifier electrocardiograph has brought clinical electrocardiography within reach of any clinician who wishes to be a student of this field, and yet the accuracy in the recording of the minute and instantaneous electric deflections has been preserved with an amazing degree of success.

*Department of Internal Medicine, Great Falls Clinic, Great Falls, Montana. Formerly, Assistant Professor of Internal Medicine, Heart Station, University Hospital, University of Michigan Medical School, Ann Arbor, Michigan.

Particularly within the past 10 years, advances in electrocardiography have been largely refinements in knowledge concerning the finer aspects of the order of ventricular excitation, and amplification of the variations that may be found in myocardial infarction, depending on its location and extent within the myocardial wall.

I intend to summarize briefly the investigative work conducted within the past decade, with special reference to three basic problems:

1. Recent investigative work indicates that a considerable portion of the inner wall of the left ventricle may be activated instantaneously and that only the outer layers of ventricular myocardium may contribute to the formation of the QRS complex at the epicardial surface.

2. There is a considerable degree of variation in the sequence of intraventricular conduction, and there may be rather marked alterations in the order of ventricular excitation without clinical evidence of organic heart disease.

3. Electrocardiographic changes of ventricular hypertrophy are not always well correlated with clinical evidence of right or left ventricular enlargement. An attempt has been made to associate these electrocardiographic changes with the physiologic changes that occur within the specific ventricle.

1. Ventricular Excitation

As early as 1915, Sir Thomas Lewis[1] in London pointed out that the specialized subendocardial network of neuromuscular tissue called the Purkinje system was capable of transmitting electric potential at a rate of 4000 meters per second or 10 times the rate of speed through ventricular musculature. He demonstrated, first in dog hearts and later in the human ventricle, that the excitation wave normally passed simultaneously into the right and left main Purkinje branches lying subendocardially on either side of the interventricular septum. Because of the speed of conduction within the network and because of the location of the specialized tissue beneath the endocardium, the inner aspect of each ventricular wall received almost instantaneous activation. The thick ventricular wall, on the other hand, was much slower to be depolarized and dependent on tangential spread of excitation from neighboring muscle lying in contact with the Purkinje network immediately beneath it. For the most part, therefore, the ventricular wall was activated perpendicularly to this conducting system from endocardial to epicardial surface.

Basic to the diagnosis of myocardial infarction is the fact that, under normal circumstances, the cavity of the left ventricle is at all times negative during ventricular depolarization. In the presence of a large transmural myocardial infarction the myocardium is electrically inert and acts as an "electric window" transmitting this negative endocardial deflection to the direct epicardial or indirect precordial unipolar lead. Problems arise, however, when the infarct is less extensive and when it may not extend throughout the entire thickness of the ventricular musculature or, more particularly, when it may involve only the subendocardial layers of the myocardium.

For many years the basic hypothesis of Sir Thomas Lewis was unquestioned. Recent investigative work has demonstrated, however, that the Purkinje network may vary in its depth of penetration within ventricular musculature so that there is great variability in the amount and depth of myocardium that may be activated instantaneously. This immediately led to the premature conclusion that infarction of such areas of myocardium, which are activated almost immediately, may be present without significant changes in leads taken over these areas.

Three groups of workers (Durrer[2] in Holland, Sodi-Pallares[3,4] in Mexico, and Prinzmetal [5-7] in the United States and their associates) have shown varying percentages of inner ventricular wall that is activated instantaneously and as a result does not contribute to the QRS complex of the electrocardiogram taken over the epicardial surface of the left ventricle. By ingenious small "stab" or "plunge" electrodes that may be moved to varying depths within ventricular muscle, they have demonstrated that 80 per cent (Prinzmetal), 66⅔ per cent (Sodi-Pallares) and 40

per cent (Durrer) of the inner wall of the left ventricle is activated almost instantaneously by the widely branching Purkinje network. By use of a single direct lead, R waves have been found to be absent in these inner layers. Bipolar leads, both located within the endocardial layers, often have demonstrated simultaneous activation or even reverse activation in the direction of epicardium to endocardium. However, Scher and his group[8-11] at the University of Washington, by use of small, delicate, paired electrodes, concluded that even the inner layers of left ventricular musculature exert definite initial forces in forming the epicardial QRS complex and are not instantaneously activated. Scher and associates pointed out a very basic fact, that even the mildest stimulation of the endocardial surface of the ventricle produces an immediate "current of injury" that is reversed in direction but identical with that in the epicardial lead.

Since the original papers by Durrer, Sodi-Pallares and Prinzmetal and their co-workers were published, these investigators have gradually reduced their estimates of the percentage of myocardium that is instantly activated. It has become apparent that Prinzmetal's "plunge" electrode, in man, may well have been in the left ventricular cavity instead of in the inner wall of the muscle mass, thus accounting for the original overgenerous estimate. One of the most difficult problems in evaluating work of this type is fixation of the "plunge" electrode within ventricular musculature. Each ventricular systole is necessarily associated with movement of muscle about the electrode. In addition, ventricular systole is associated with thickening of ventricular musculature, so that fixation of such an electrode on the surface of the heart may necessarily result in considerable variation in the location of the tip of the electrode within the muscle during one complete cardiac cycle.

To summarize the investigative work concerning instantaneous activation of the left ventricular wall, the question whether the Purkinje fibers do or do not extend into the wall of the ventricle remains unanswered, but to date it has not been demonstrated anatomically that they do. Whether the free wall of the ventricle is activated in the chaotic manner suggested by Prinzmetal, with only a shell of outer myocardium contributing to the QRS complex, or whether the concept of radial spread through ventricular muscle as suggested originally by Lewis is correct is still being investigated. In any event, the challenge of the long-accepted hypothesis of Lewis has been beneficial in pointing out that in the presence of small endocardial infarcts the changes may be less than those described with classic myocardial infarction, and that infarction may be suspected from relatively minor *serial* changes in the electrocardiogram. The statement that postmortem examinations occasionally demonstrate definite small infarcts (usually subendocardial in location) in cases in which the electrocardiograms were entirely normal is in no way an argument to support the new hypothesis. It merely points out the need and desirability of serial records and of additional exploratory chest leads whenever infarction is suspected clinically and the conventional tracing is within normal limits. The basic concept concerned with the origin of the changes seen in the presence of myocardial infarction has not been challenged.

2. Intraventricular Conduction

The second problem in electrocardiography which I wish to discuss concerns the important question of intraventricular conduction. Again referring to Sir Thomas Lewis's original work in the early part of this century, and also to the contributions of Frank Wilson and his associates, it has been clearly shown that the upper portion of the interventricular septum is activated initially from left to right because of the earlier branching of the left bundle of His. The lower portion of the septum is activated from both bundles, so that simultaneous forces from the left and from the right side of the endocardial surfaces oppose each other. In the sequence of activation both the free wall of the right ventricle and the free wall of the left ventricle are then simultaneously activated from endocardial to epicardial surfaces as the electric stimulation passes rapidly through the Purkinje network. Because of the greater thickness of the left

ventricle and because of the relatively greater distance of part of the left ventricular musculature from the ventricular septum, the latter forces become predominant and constitute the last portion of the heart to be depolarized. This sequence of classic intraventricular conduction has been termed by Bryant and Kossmann[12] "initial left septal-late left mural activation." It is characterized by the following QRS configurations:

Cavity of right ventricle—Initial positivity due to activation of the upper portion of the interventricular septum from left to right, followed by a deep S wave, due to right and left ventricular wall activation.

Cavity of left ventricle—A deep QS deflection due to forces away from the cavity of the left ventricle at all times.

Epicardial surface of right ventricle—Initial positivity due to upper septal forces from left to right plus activation of the free wall of the right ventricle beneath the electrode, followed by a deep S wave resulting from activation of the thicker left ventricular wall in an opposite direction.

Epicardial surface of left ventricle—Initial negative deflection due to septal influence from left to right followed by a large R wave due to depolarization of the left ventricular musculature beneath the electrode.

Bryant and Kossmann,[12] in an extensive study of the electrocardiograms of normal and abnormal subjects, found that this so-called normal conduction occurred infrequently in normal persons and frequently in those with clinical evidence of heart disease. Although the details of how often this paradox may occur are unimportant, this study points out very well the frequency with which minor variations in intraventricular conduction may occur and the necessity of recognizing them as variations of normal conduction. It has become apparent that many persons have been labeled as having heart disease and have been denied life insurance on this basis, without just reason. The presence of these minor variations in intraventricular conduction, in the absence of other electrocardiographic abnormalities or of clinical evidence of organic heart disease, does not justify this conclusion.

These minor variations in intraventricular activation fall into two major groups: late activation of portions of the right ventricle, and variations in activation of the initial portion of the septum from right to left, rather than the reverse. It has been recognized for some time that portions of the right ventricular musculature about the pulmonary conus in the region of the crista supraventricularis are located at a distance farthest from the basal portion of the interventricular septum. It is thus understandable that completion of activation of this portion of the right ventricle may constitute the last phase of depolarization of the heart. This finding accounts for the frequent appearance of late secondary R waves in leads taken over the free wall of the right ventricle, and for the frequent electrocardiographic diagnosis of incomplete right bundle-branch block. In view of such a physiologic variation, the diagnosis of block seems unjustified and unwarranted when in reality we are dealing with a normal variant in the sequence of ventricular activation.

Bryant and Kossmann estimated that 85 per cent of their normal subjects had some variation of this latter form of conduction. In 1954, Johnston and I[13] pointed out the value of additional chest leads, both to the right of the conventional precordial leads (V_{3R} and V_{4R}) and above the usual V_1 and V_2 position (V_1 and V_2 in the second intercostal space), in clarifying the significance of this electrocardiographic finding.

In addition to these variations in the late stages, variations in the early phases of ventricular activation have also been recognized recently. It has been well established that at least a portion of the base of the ventricular septum is activated from below upward. Likewise, initial septal influences may occur from right to left, rather than the reverse, or may occur simultaneously from both epicardial surfaces. This situation results in initial positivity within the cavity of the left ventricle and disappearance of initial negativity over the free wall of the left ventricle due to early right septal activation. This electrocardiographic finding alone, in the absence of prolongation of the QRS interval, need not con-

stitute an abnormality. More work needs to be done to clarify the variations in initial septal activation and the electrocardiographic picture of incomplete left bundle-branch block. Differentiation of the latter abnormality from left ventricular hypertrophy likewise remains a difficult problem in electrocardiography.

In interpreting electrocardiograms, one should appreciate the variation that may occur in the sequence of ventricular activation and be slow to label these variations as abnormalities of block.

3. Ventricular Hypertrophy

Analogous to the problems of spread of excitation and intraventricular conduction is the problem of myocardial hypertrophy. The criteria of left and right ventricular enlargement are not clearly defined. In general there appears to be closer correlation of clinical evidence with the electrocardiographic diagnosis of hypertrophy than with the radiologic evidence of ventricular enlargement. Numerous studies have been conducted correlating the electrocardiographic picture of hypertrophy with postmortem evidence of thickening of the ventricular wall. Although the results of these studies are variable, in general a 70 per cent correlation of the electrocardiogram with clinical evidence of hypertrophy is found. It is of interest that a higher percentage of agreement is found when electrocardiograms showing either right or left ventricular hypertrophy are selected and then compared with necropsy material than is found when routine autopsy material with hypertrophy is selected and electrocardiograms are compared with this material. It is for this reason that any percentage of correlation is practically meaningless.

Of interest in recent years has been the attempt to correlate the electrocardiographic picture of hypertrophy with the circulatory dynamics of the heart. The concept of "overloading," first introduced by Cabrera and Monroy[14] in 1952, was amplified to a considerable extent by Sodi-Pallares and Marsico.[15] The basis for this concept was the belief that hypertrophy of cardiac muscle occurred not only from increased diastolic length of the muscle fiber (as defined by Starling's law) but also from contraction against an increased tension or resistance. For example, in aortic valvular disease, pure aortic insufficiency results in increased diastolic filling of the heart due to the inability of the incompetent aortic valve to prevent part of the ejected blood from regurgitating back into the left ventricle. This load, in addition to the usual diastolic filling from the left atrium, results in a marked increase in diastolic volume within the left ventricle. In contrast, in pure aortic stenosis there is no increased diastolic volume early but rather an increased intraventricular pressure with concentric hypertrophy to overcome obstruction at the outflow orifice. The electrocardiographic changes seen with these pathologic states are as follows:

Left ventricular diastolic overload (aortic insufficiency)—Large prominent R waves with upright and often high T waves. The important feature here is that the ventricular gradient is normal.

Left ventricular systolic overload (aortic stenosis)—S-T segment depression with inverted T waves resulting in a decreased or absent ventricular gradient.

Right ventricular diastolic overload (interatrial septal defect)—Classic right bundle-branch block with late activation of the right ventricle.

Right ventricular systolic overload (pulmonic stenosis)—Prominent R waves in leads over the right ventricle without delay in intraventricular conduction.

Despite the obvious desirability of correlating the altered physiologic state and the electrocardiographic picture, it is obvious that these concepts are not always true. More importantly, the clinical picture often is more complicated, with combinations of both systolic and diastolic overloading, e.g., combined aortic stenosis and aortic insufficiency. Undoubtedly factors other than myocardial work play an important part in the electrocardiographic picture that is obtained. One may conclude that the correlation between clinical evidence and electrocardiographic evidence of ventricular hypertrophy is lacking occasionally and that to date a satisfactory ex-

planation for this discrepancy has not been offered.

Comment

The three problems I have discussed constitute the major problems in electrocardiographic research today. More emphasis in recent years has been directed toward the graphic recording of the vectorcardiogram. In many respects this field is reduplicating many of the problems electrocardiographers faced several years ago, particularly with reference to establishing a satisfactory and universally acceptable system for the horizontal, vertical and sagittal components. Whether or not the vectorcardiogram will attain the clinical position of the electrocardiogram remains to be seen. It would seem at this time that basically the vectorcardiogram, like the ballistocardiogram, is a research tool and not of sufficient additional clinical value to displace the conventional electrocardiogram.

All of these graphic methods are laboratory aids in the diagnosis or exclusion of organic heart disease, and as such they may, on occasion, conflict with the clinical opinion based on the history and physical examination. Altogether too often they are used as substitutes or "short cuts." It is unfortunate that the attention of the average layman has been so directed toward the electrocardiogram that many times he feels the cardiac evaluation is incomplete unless his physician elects to obtain the tracing. Knowledge that the electrocardiographic interpretation may vary among different physicians is not well appreciated.

Davies[16] found that when 100 electrocardiograms were circulated among nine competent interpreters there was complete agreement in only about one-third of the interpretations and major agreement in about half of them. Even more interesting was the finding that when the tracings were redistributed to the same observers some time later the interpretations differed significantly from the original ones in an average of one out of eight instances. This serves to re-emphasize the importance of the history and significant physical findings in interpretation of electrocardiograms.

REFERENCES

1. Lewis, T.: The spread of the excitatory process in the vertebrate heart. Parts I to V. Phil. Trans. Roy. Soc. 207:221, 1916.
2. Durrer, D., van der Tweel, L. H., Blickman, J. R., Berreklouw, S. and van der Wey, L. P.: Spread of activation in the left ventricular wall of the dog. Am. Heart J. 46:683, 1953. Activation conditions at the epicardial surface. *Ibid.* 47:192, 1954. Transmural and intramural analysis. *Ibid.* 48:13, 1954. Two and three dimensional analysis. *Ibid.* 50:860, 1955.
3. Sodi-Pallares, D., Barbato, E. and Delmar, A.: Relationship between the intrinsic deflection and subepicardial activation; an experimental study. Am. Heart J. 39:387, 1950.
4. Sodi-Pallares, D., Bisteni, A., Medrano, G. A. and Cisneros, F.: The activation of the free left ventricular wall in the dog's heart. Am. Heart J. 49:587, 1955.
5. Massumi, R. A., Goldman, A., Rakita, L., Kuramoto, K. and Prinzmetal, M.: Studies on the mechanism of ventricular activity. XVI. Activation of the human ventricle. Am. J. Med. 19:832, 1955.
6. Kennamer, R. and Prinzmetal, M.: Depolarization of the ventricle with bundle-branch block. Studies on the mechanism of ventricular activity. Am. Heart J. 47:769, 1954.
7. Kennamer, R., Bernstein, J. L., Maxwell, M. H., Prinzmetal, M. and Shaw, C. M.: Studies on the mechanism of ventricular activity. V. Intramural depolarization potentials in the normal heart with a consideration of currents of injury in coronary artery disease. Am. Heart J. 46:379, 1953.
8. Scher, A. M., Young, A. C., Malmgren, A. L. and Paton, R. R.: Spread of electrical activity through the wall of the ventricle. Circulation Res. 1:539, 1953.
9. Scher, A. M., Young, A. C., Malmgren, A. L. and Erickson, R. V.: Activation of the interventricular septum. Circulation Res. 3:56, 1955.
10. Scher, A. M. and Young, A. C.: Spread of excitation during premature ventricular systoles. Circulation Res. 3:535, 1955.
11. Erickson, R. V., Scher, A. M. and Becker, R. A.: Ventricular excitation in experimental bundle-branch block. Circulation Res. 5:5, 1957.
12. Bryant, J. M. and Kossmann, C. E.: Intraventricular conduction. In Advances in Electrocardiography. New York, Grune & Stratton, Inc., 1958, chap. 10.
13. Overy, D. C. and Johnston, F. D.: The use of additional chest leads to estimate the significance of electrocardiograms that suggest incomplete right bundle-branch block. J. Lab. & Clin. Med. 44:905, 1954.
14. Cabrera, C. E. and Monroy, J. R.: Systolic and diastolic loading of the heart. I. Physiologic and clinical data. II. Electrocardiographic data. Am. Heart J. 43:661;669, 1952.
15. Sodi-Pallares, D. and Marsico, F.: The importance of electrocardiographic patterns in congenital heart disease. Am. Heart J. 49:202, 1955.
16. Davies, L. G.: Observer variation in reports on the electrocardiogram. Brit. Heart J. 20:153, 1958.

Reactions of Medical Patients to Discharge or Threat of Discharge From a Psychosomatic Unit of a General Hospital

STANLEY M. KAPLAN AND GEORGE C. CURTIS*

University of Cincinnati College of Medicine, Cincinnati

Introductory Comment

This is an extremely interesting article and, I think, widely applicable to the adjustment problems of hospital discharge which are faced by the patients of physicians in all specialties. As the authors remark, the routine medical or surgical patient, hospitalized briefly and in relative isolation from other patients, may not experience the intense reactions to discharge which occur in patients in the particular psychosomatic unit studied. However, it must be remembered that any illness warranting hospitalization involves some decompensation of personality adjustment. During the period of illness, the patient cannot cope with his daily environment and relies on the care administered by other people. Intensified dependency needs, regressive trends, and some injury to self-confidence are an intrinsic part of debilitating illness. Thus, any patient faces a measure of demand for personality reintegration following discharge from the hospital. To the extent that these emotional problems are recognized and adequately managed, the patient's recovery from his illness will be facilitated.

The research is, of course, directly applicable to psychiatric hospitals, where the relationships and interdependency factors among patients and between patients and staff are necessarily intense. This is a major argument for the "open hospital" program, which can be preventive in maintaining some of the patient's identifications within the community and can be rehabilitative in providing a means of slowly weaning the patient away from the hospital. It also points up the need for administrative integration of psychiatric hospitals and community clinics, so that the patient's physician may participate in aftercare, and hospital discharge will not also mean the sudden severing of a patient-physician relationship which may have intense meaning for the patient.—Franklin G. Ebaugh, M.D.†

*Department of Psychiatry, University of Cincinnati College of Medicine, and the Psychosomatic Service of the Cincinnati General Hospital, Cincinnati, Ohio. Dr. Curtis is now at the Eastern Pennsylvania Psychiatric Institute and Clinic, Philadelphia, Pennsylvania.

†Editorial Consultant in Psychiatry, POSTGRADUATE MEDICINE; Emeritus Professor of Clinical Psychiatry, University of Colorado School of Medicine, Denver, Colorado.

STANLEY M. KAPLAN

GEORGE C. CURTIS

PATIENTS usually urge their physicians to discharge them from the hospital as soon as possible. Their attitude is that they dislike remaining in the institution and prefer being at home. Yet, it is not uncommon for physicians to observe some patients who procrastinate about leaving the institution; in other patients either exacerbations of physical symptoms occur or new symptoms develop which necessitate delaying discharge. There also are times when the patient's reluctance to leave the hospital is not evident to the medical staff and, indeed, is hidden from the patient himself. It is important, therefore, that the physician and others of the hospital staff recognize the problems that may arise at the time of discharge, deal with them as effectively as possible, and thereby minimize any resulting impact on the patient's health and the staff's morale.

This report is based on our observations over a number of years of the psychologic and physiologic reactions of medical patients at the time of discharge or at the threat of discharge from the psychosomatic unit of the Cincinnati General Hospital. The patients on this 12 bed unit are men and women with physiologic disorders of various types. Ordinarily, they are not acutely ill, but usually they have experienced illness over a moderately long period. Most of the conditions observed are classified diagnostically within the psychophysiologic autonomic and visceral category, e.g., hypertension, peptic ulcer, neurodermatitis, diabetes, asthma, ulcerative colitis and the like. However, other types of medical disorders are represented, and some of the patients have symptoms referable to their physical state which are principally psychologic, such as occur in conversion, depressive and schizophrenic reactions. Most of the patients are from the low socioeconomic segment of the population which is served by this municipal general hospital, but some of them have been referred by private hospitals and practitioners to obtain the benefits of a comprehensive approach. The patients are assigned to a single room, a two bed room, or a five bed room, depending on their needs and on the accommodation available. They spend much of their time in a day room, but at times they leave the ward for occupational therapy or to go home on pass. When preparing for discharge, they may go out to look for work. The average hospital stay is approximately two months, with a range of from several weeks to a year. During this time, patients are studied comprehensively in terms of their psychophysiologic states. The patients are in both individual and group psychotherapy, and the small size of the unit affords an opportunity for very close observations of individual behavior and of the group interaction.

Benedek[1] pointed out that the process of separation involves both the person leaving and those from whom he departs. Accordingly, reactions to discharge, i.e., separation from the hospital, may be seen in terms of the patient who is being discharged, in terms of the remaining patient group which is losing one of its members, and in terms of the staff members who have invested time and energy in treating the departing patient.

The Patient Being Discharged

In one consecutive series of 35 patients who were specifically observed for discharge reactions, about half of them revealed some observable difficulty at this time. Some of the patients reacted to the prospects of discharge principally in a psychologic manner; others reacted mainly with physiologic change, while still others clearly demonstrated both aspects of the total organismic response. Psychologic reactions ranged from mild depression and concern about ability to return to productive work to enraged indignation over being "kicked out like a stepchild" and exacerbation

of a previous pattern of delusional thinking. Physiologic reactions ranged from coryza to serious febrile reactions (in a patient with an unspecified disease of the reticuloendothelial system) and to death due to the advent of a cardiovascular accident (in a patient with severe hypertension).

The severity and the kind of reaction to discharge depend on a number of factors, but conspicuous among these are (1) basic personality structure of the patient; (2) type and severity of the patient's illness; (3) duration of hospitalization; (4) the physician-patient relationship that has developed during hospitalization and the anticipated fate of this relationship after discharge; and (5) the situation the patient must enter following discharge from the hospital. There are a variety of determinants, and many are operating at the same time in any individual patient.

The following case excerpts are selected to illustrate some of these five factors.

Case reports—Case 1—A patient who had had a mitral commissurotomy because of rheumatic heart disease was referred to us because of her poor adjustment following surgery. She was interviewed on several occasions as an outpatient. A history of recurring upper respiratory infection led us to admit her to the ward for psychotherapy and as a subject for a research project.

The patient seemed quite willing to come into the hospital, particularly since she had felt anxious and was indeed dissatisfied with the two key interpersonal relationships in her life. Her adjustment with her husband was poor. She saw him as "unattractive and crude," and the idea of sexual intercourse with him was "repulsive" to her. The patient alternately lived with her husband and with her mother, with whom she also was disappointed and angry, especially because of her mother's close relationship with a man the patient described as a "weak drunkard who let Mother run his life for him."

Her adjustment on the psychosomatic unit was erratic. Although it was evident to her and others that she enjoyed the care and protected atmosphere of the hospital, the intensity of her demands to receive often led to friction with the other patients and with the nursing staff. She would complain to her therapist that she was being denied medications, attention by the nurses, and such. Psychologic studies indicated that she was an egocentric, hysteric individual who, on a deeper level, had intense dependency wishes and craved a closeness with her mother which she felt she never had had. She remained on the unit for 10 months. The therapeutic plan involved an attempt to give her some insight into her problems as well as to arrange for vocational rehabilitation. She rarely complained about the length of her hospital stay. When she was about to be discharged, it was evident that she was reluctant to leave, and she found many excuses for remaining in the hospital "a little while longer." She said she wished further time to work out living arrangements and angrily complained and threatened that all our efforts to rehabilitate her would be for nought if she was to be upset about this. The extra time to work out these arrangements and the assistance given by our social worker inevitably proved fruitless, and it was only with considerable pressure on the part of her therapist that she agreed to leave.

A year later, this patient was again admitted, but it was agreed beforehand that this was to be for a maximal hospitalization of three weeks to repeat the experiment in which she had participated the previous year. She protested mildly and she wanted specific assurance that she would not have to stay longer. Three weeks later, at the time of her discharge, she became intensely angry. She complained that she had been exploited and was being "discarded" now that the research was over. There were other outbursts of anger over petty matters, which alternated with periods of passive compliance with all the personnel's requests. She complained that she was not well enough to leave and virtually pleaded to be allowed to remain until she could get her own apartment, which her mother was to finance. During several interviews, her anger became intense; she cried, left the office, and said she would never return to the hospital or to see the therapist again. It was apparent that hospitalization would have to be extended. She

began to fibrillate and also experienced a mild thrombophlebitis. The intensity of her anger was such that the staff felt it advisable to keep her longer to allow for a ventilation of the anger and thereby to keep intact the physician-patient relationship. Finally, just prior to discharge (six weeks after admission), a slight pitting edema of the legs developed, and she experienced some pulmonary congestion. This responded to diuretics, but it represented the most serious signs of cardiac decompensation we had seen in this patient. Discharge symptoms later abated.

Comment—It is evident that several factors contributed to the psychologic and physiologic reactions this patient experienced with the threat of discharge from the hospital. Her personality structure was such that hospitalization satisfied, in a way she could justify, her strong wishes for care and protection. The type of illness, i.e., rheumatic heart disease, provided a vulnerability to arrhythmia and to congestive heart failure. The physician-patient relationship was an intense one in which the patient became excessively dependent on the physician and staff, a situation which was unduly fostered by the physician's feeling of a need to "repay" the patient for her participation in his research project. This latter factor probably caused the physician to permit the patient hospitalization beyond an optimal period. The situation which the patient was reluctant to enter on leaving the hospital involved either living with her husband and facing the rage over the implied sexual demand or living with her mother and facing the shame over her childlike wishes for care and protection.

Case 2—A 53 year old married woman had had severe hypertension of the order of 240/110 to 280/160 for at least 12 years. For approximately the same period, she had had attacks of anxiety and throbbing headaches. She was hospitalized for treatment of the hypertension, signs of which suggested an early malignant phase. Hypotensive agents plus individual psychotherapy and milieu therapy provided some slow but definite improvement over a period of several months. In the process, she became intensely attached to her therapist. Unfortunately, the therapist, an Italian citizen, was forced to return to his native country on very short notice. The patient was informed of this and of the decision that she would be discharged from the hospital in the outpatient care of another physician. She was extremely distressed about the impending loss of her doctor. Two days after the patient was informed of the decision, impairment of speech and hemiplegia on the right side developed; she died eight days later.

Comment—Certainly, the type and severity of this patient's illness and the type and fate of the physician-patient relationship that developed in the hospital, in terms of sudden, unexpected disruption coincident with the plan for discharge, contributed to the patient's cerebrovascular accident and ultimate death. A more physically intact person could have withstood the impact of this psychologic stress without experiencing a similar fate.

Case 3—A 56 year old spinster had had a mild agitation and depression several months prior to being admitted to the hospital. These symptoms intensified when it was later discovered that she had chronic lymphocytic leukemia. The patient had been living alone, supporting herself well for the previous 14 years as a typist. She had had one previous bout of depression when she was 16 years old, following her mother's death. She always had said, "When Mother dies, I want to die." The patient's mother was 56 years old when she died, which was the patient's age when she was admitted to our unit.

In the hospital, the patient clung to the nurses, constantly sought reassurance, and often felt others disapproved of her. However, with the protection of the hospital, sedation, and supportive psychotherapy, her depression subsided. After six weeks on the unit, it was thought that her recovery was adequate and plans were made for her to return to work. She was afraid to leave the hospital and return to her job, since she did not feel self-confident and feared she would make a number of errors at work and be dismissed. These prospects of failing seemed quite frightening to her, and the therapist postponed discharge. It was then decided that she should remain in the

hospital while going out to work for initially brief but then increasingly longer periods of the day. Her employer agreed to this plan without hesitation. The first day at work, the patient had an attack of nausea and returned immediately to the hospital. With gentle urging, she went back to work the next day and met with some success. With increasing success each day, she gradually reorganized and ultimately resumed her previous mode of adjustment to life.

Comment—Several factors entered into this patient's difficulty at the time of discharge from the hospital. Prior to the onset of her illness she had found ample solutions to her personality problems and had made a reasonable adjustment to life. By the time of hospitalization these effective personality adjustment mechanisms had crumbled and overt problems were present. Leaving the hospital necessitated a reintegration of personality structure. The problem was complicated by the fact that there were no good sources of support outside the hospital to assist her during this transition period. She lived alone and had no close friends or family. The best source was her employer; however, she feared jeopardizing this relationship. The discharge was ultimately successful when it was accomplished gradually by the staff, almost in a "weaning" manner.

Reactions of the Remaining Group

The patient group on the psychosomatic unit frequently reacts to the discharge of one or more of its members, since it reminds them that they, too, will have to face the problems involved in leaving the hospital at some future time. Rather characteristically, the nurses' interaction reports, which describe the major events on the unit and predominant theme of conversation by the patients, reflect this. For example, "Patient L. leaving today; there appears to be a great deal of tension among the group as to who is going to be discharged in the near future." Another report read, "Talk of all the discharges. Speculation after each leaves as to how he will get along on the outside."

The remaining patients seem uncertain about the security of their relationships with the staff and the hospital in general at these times. Their behavior then often changes in a manner calculated to insure perpetuating the relationships. For example, evidences of anger, discontent or dissatisfaction which had been previously expressed often are squelched or concealed from the staff. Group pressure will be exerted against patients who are inclined to misbehave and thereby threaten to arouse anger in the staff. There frequently is an increase in somatic complaints as a bid for individual attention.

The others in the group often try to be helpful to the departing member, perhaps out of guilt over getting rid of someone with whom they had to share the staff's care and attention. If the person who is leaving has been a leader for the group, more specific reactions may arise, such as loss of cohesiveness or organization of the group.

Some comments from a group meeting at a time when several patients were being discharged were as follows:

Patient T. wanted to leave the hospital, but now that the time has come she "hates to go." Patient P. wants to go but "hates to." "They did a lot for me here. I like the people. It's a little like home and it hurts to go, but I'm needed badly at home." Mrs. A. "frankly admits" that the idea of eventually leaving bothers her. Mrs. T. then says, "You do hate to admit you hate to leave the hospital." Mrs. N. wants to go but feels "afraid and funny about it." Mr. M. asks whether the others think that "in some cases, but, of course, none here, while on N-3 [the ward] you get your thinking done for you. You keep your room up a bit, but after three months you hate to face everyday life again."

An individual patient's reaction to the discharge of another patient was described by her some time later during an interview. "The night before Mrs. C. was supposed to leave, she read Bible verses and sang hymns and spiritual songs. I asked her to sing them. I cried when she did. She was doing it for me and for the others. I knew by her doing it that she did like me. It made me relax more; I was trying to keep from crying. I hated to

see her leave. I didn't want to be hurt by her leaving."

It is evident that the patients have reactions to the discharge of other patients, as well as to their own discharge. These are at times similar to grief reactions.

Reactions of the Staff

The professional staff obviously must be considered in relation to discharge reactions, since they decide the time and manner of the patient's discharge. Their attitudes at this time may play a large part in the patient's reactions and the fate of the patient's illness after discharge. For example, unnecessary delay in discharging the patient may reflect the staff's guilt over some neglect or dislike of the patient. On the other hand, excessive hospitalization may be the physician's response to childish, plaintive or seductive attitudes on the part of the patient.

At other times, an unnecessary urgency to discharge the patient before he is adequately prepared for it may reflect reactive anger at an uninteresting patient or one who subtly provokes and taxes the patience of the physician. A sign-out without recommendation by the staff, a decision seemingly made by the patient, is sometimes unconsciously encouraged for any variety of reasons by the physician in charge. We also have noted that disharmony among the staff members may be the cause or the result of discharging a patient.

Discussion

Our patients may experience greater difficulty than some other medical patients at time of discharge because of their relatively lengthy hospitalizations, their excessive exposure to basic frustrations in their early lives, or a certain indulgence of their dependency needs and reduction of life stresses while in the hospital. Many of the observations described here will be unique to hospital units organized in a manner somewhat similar to ours. Thus, reactions of patients who are more or less isolated from all other patients and who remain in the hospital for a very brief time may be distinctly different. However, many of the factors described here also may be found at work in other hospital populations. This is especially so now and probably will be even more evident in the immediate future, since hospitalization is being used for an increasingly larger number of long-term care patients while the acute disorders are becoming increasingly amenable to office treatment.

Perhaps it should not be surprising that a sizable percentage of our patients, and probably others as well, react adversely to discharge, since this event is of the type that often strikes at the core of basic psychologic needs. In fact, for many patients, discharge echoes the stress they encountered which precipitated the onset or exacerbation of the ailment that brought them into the hospital. Separation, loss of dependency satisfactions (symbolic or real), or a threat of such loss is commonly found in the lives of patients, prior to the onset of illness. The loss of key persons in the lives of patients, leading to the onset or exacerbation of disease, has been reported by many, including Engel,[2] Lindemann,[3] Greene and Miller[4] and Schmale.[5] It is apparent their findings apply to our patients when one recognizes that the doctor or some other staff member is indeed a key person in the patient's life. When the relationship is maintained and when it is a source of some gratification to the patient, it can be a powerful factor for symptom relief. However, if this must be terminated abruptly, it can prove to be two-edged.

Failures in handling the discharge period can have deleterious effects on the staff as well as on the patients. Recurrence of symptoms may reflect in a feeling of failure by the staff, thereby lowering staff morale and, secondarily, causing them to reject the patient angrily, throw up their hands in despair, and decide that it is impossible to help the patient.

We have used a variety of technics to smooth the transition from hospital to home, both in the hospital with patients and staff and in relation to family and community through social service.

There are particular advantages to discussing openly with the patient his feelings about discharge. It permits ventilation of the patient's feelings, more specifically of his fears

about leaving the hospital and his anger toward the doctor, who he may think is abandoning him. These feelings, which otherwise may be kept below the surface, often can be elicited if the doctor just sits with the patient for an added period when the subject of discharge is brought up, thus affording the patient an opportunity to express his feelings. A casual comment implying that patients may have mixed feelings about leaving may be sufficient to reduce any shame the patient may have about discussing the matter. Open discussion also brings to the attention of the staff members the need to consider the patient's emotional and physical reactions in this transition. In addition, more realistic plans, which are in keeping with the patient's physical and emotional needs and resources on the outside, can be made with the help of social service. For example, a matter as simple as making certain that an elderly cardiac patient or his family understands how frequently he should take his digitalis can be of lifesaving importance.

In conclusion, we would like to cite Mann's[6] description of a patient's dilemma over leaving the hospital. The speaker is Settembrini, who is talking to Hans Castorp; both are at a mountain sanatorium for tuberculous patients. "I myself have seen some beautiful cases of acclimatization. There was *Fräulein* Kneifer, Ottilie Kneifer, last year. She came of a good family—the daughter of an important government official. She was here some year and a half and had grown to feel so much at home that when her health was quite restored—it does happen, up here; people do sometimes get well—she couldn't bear to leave. She implored the *Hofrat* to let her stop; she could not and would not go; this was her home, she was happy here. But the place was full, they wanted her room, and so all her prayers were in vain; they stood out for discharging her cured. Ottilie was taken with high fever, her curve went well up. But they found her out by exchanging her regular thermometer for a 'silent sister.' You aren't acquainted as yet with the term; it is a thermometer without figures which the physician measures with a little rule and plots the curve himself. Ottilie, my dear sir, had 98.4°; she was normal. Then she went bathing in the lake—it was the beginning of May; we were having frost at night; the water was not precisely ice-cold, say a few degrees above. She remained some time in the water, trying to contract some illness or other—alas, she was, and remained, quite sound. She departed in anguish and despair, deaf to all the consolations her parents could give. 'What shall I do down there?' she kept crying. 'This is my home!' "

Summary

Although patients usually press for discharge from the hospital, leaving the institution may be psychologically stressful. The stress of this transitional period may have deleterious effects on the patient's psychologic or physiologic state or both. It is important that physicians and hospital personnel in general be aware of the patient's dilemma at this time and assist him in his adjustment to this transition.

REFERENCES

1. Benedek, T.: Insight and Personality Adjustment: A Study of the Psychological Effects of War. New York. The Ronald Press Company, 1946.
2. Engel, G. L.: Studies of ulcerative colitis: III. The nature of the psychologic process. Am. J. Med. 19: 231, 1955.
3. Lindemann, E.: Psychiatric problems in conservative treatment of ulcerative colitis. Arch. Neurol. & Psychiat. 53:322, 1945.
4. Greene, W. A., Jr. and Miller, G.: Psychological factors and reticuloendothelial disease: IV. Observations on a group of children and adolescents with leukemia: An interpretation of etiopathogenesis in terms of the mother-child unit. Psychosom. Med. 20:124, 1958.
5. Schmale, A. H., Jr.: Relationship of separation and depression to disease. I. A report on a hospitalized medical population. *Ibid.*,[4] p. 259.
6. Mann, T.: The Magic Mountain. New York. Alfred A. Knopf, Inc., 1951.

Anatomy for Surgeons

E. A. BOYDEN*

University of Washington School of Medicine, Seattle

E. A. BOYDEN

In these days, when the time allotted to the teaching of gross anatomy in our medical schools is being curtailed so drastically, the anatomist must find new ways of presenting the fundamental patterns of the body and of relating these to clinical objectives.

Using the lungs as an example, one may ask, "What is the most important anatomic approach to this subject?" Eventually, to be sure, the prospective surgeon must acquire a detailed knowledge of the segmental organization of the lungs and of the ways in which advance information about the anatomy of the patient may be obtained from such diagnostic aids as x-rays, bronchography and bronchoscopy. When he starts operating, however, his chief source of information will be the anatomy which is revealed by the structures in the hilus or root of the lung. Then why not start with the anatomy of the hilus?

With this in view, I prepared the series of dissections of the cadaver illustrated in chapter 1 of "Diseases of the Chest Including the Heart" by J. A. Myers (Charles C Thomas, Springfield, Illinois, 1959). During the course of this work, problems relating to the surgery of the lungs were discussed with a former graduate student, Dr. Franklin R. Smith, now a skilled thoracic surgeon in Seattle. Inevitably, the next step was to portray the living anatomy of the hilus. A grant to the department of medical illustration of the University of Washington School of Medicine provided the necessary means for surgeon and anatomist to attack this problem together.

The objective was to photograph and elucidate the anatomy of the hilus as revealed by minimal dissection of the anterior, posterior and interlobar surfaces of the root of the lung whenever suitable operations provided the necessary exposures. Selected frames from the films were then "blown up," and drawings of these were made by the artist. In this way, a teaching film was prepared in which the anatomy displayed in the explanatory figures was that of the patient who was filmed, not merely textbook anatomy. Throughout the film, the emphasis is on the anatomy that the surgeon must know in order to carry out the given surgical procedure.

The four drawings from the film presented here indicate the point of view used in the film. By such means, the student of surgery is taught where to find the structures that have to be ligated and divided in segmental resection, lobectomies, etc. Obviously, in the course of the film, certain surgical technics are shown, but the emphasis throughout is on the anatomy of the pulmonary hilus and its relation to the bronchopulmonary segments.

*Professor Emeritus, Department of Anatomy, University of Minnesota Medical School, Minneapolis, Minnesota; Research Professor, Department of Anatomy, University of Washington School of Medicine, Seattle, Washington.

Adapted from a presentation in a course on Emergency Surgery for General Physicians at the University of Minnesota Center for Continuation Study, Minneapolis.

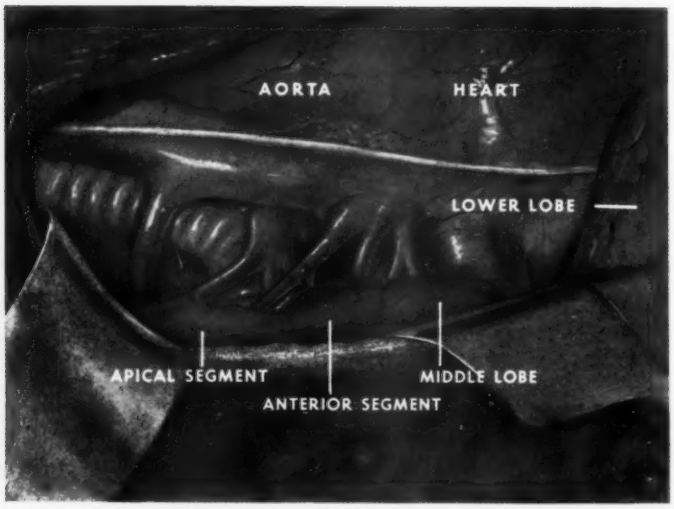


FIGURE 1.

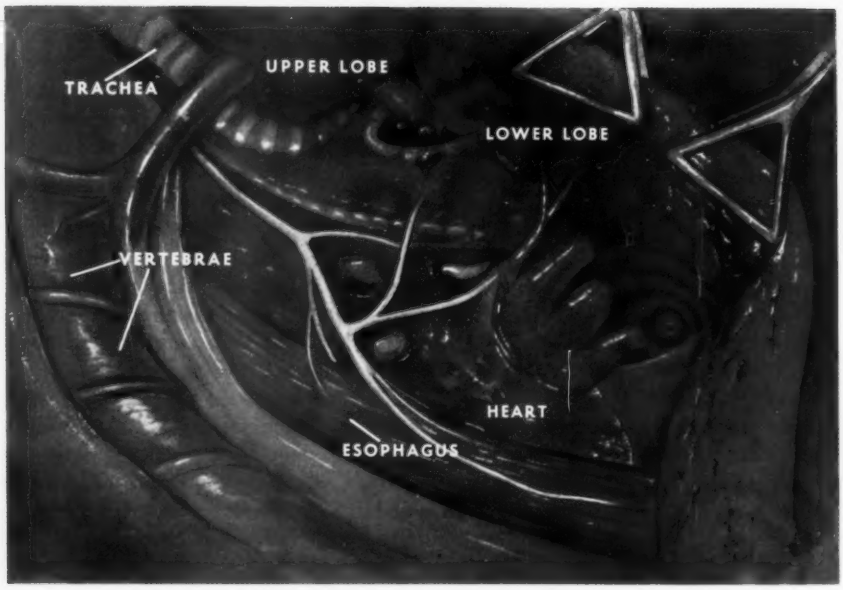


FIGURE 2.

FIGURE 1. Dissected anterior surface of the hilus in a patient. Beginning on the left, one sees the superior vena cava overlaid by the right phrenic nerve and underlaid by the trachea; the azygos vein arching over the root of the lung; the upper lobe bronchus; the anterior trunk of the right pulmonary artery giving off rami to the apical and anterior segments; the right superior pulmonary vein receiving tributaries from the apical, anterior and middle lobe segments; and, finally, the right inferior pulmonary vein draining the lower lobe.

FIGURE 2. Posterior mediastinum and posterior aspect of the hilus after the right lung has been elevated. Beginning at the left, one sees the azygos vein crossing the trachea; the right main bronchus giving off the upper lobe bronchus, which later is crossed by the ascending artery to the posterior segment; the lower lobe bronchus; and, beyond that, the right inferior pulmonary vein, with tributaries from the superior and basal segments of the lower lobe. Below these structures may be seen the aorta, the esophagus, and the branches of the right vagus nerve.

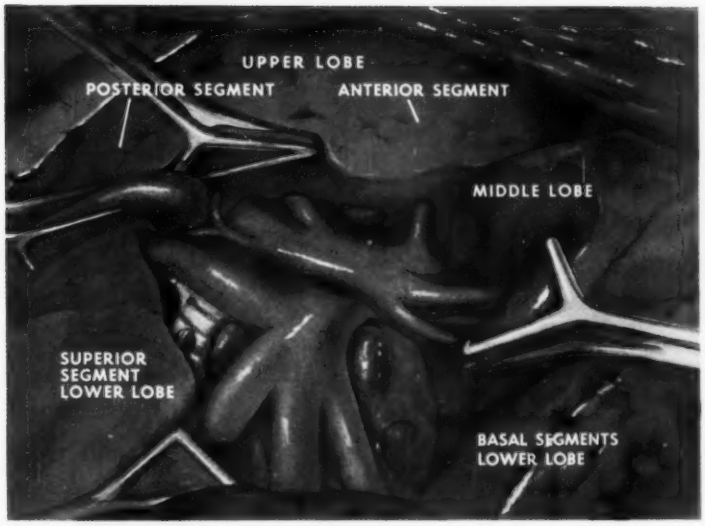


FIGURE 3.

Drawings by Jessie W. Phillips, Head of Department of Medical Illustration, University of Washington School of Medicine.

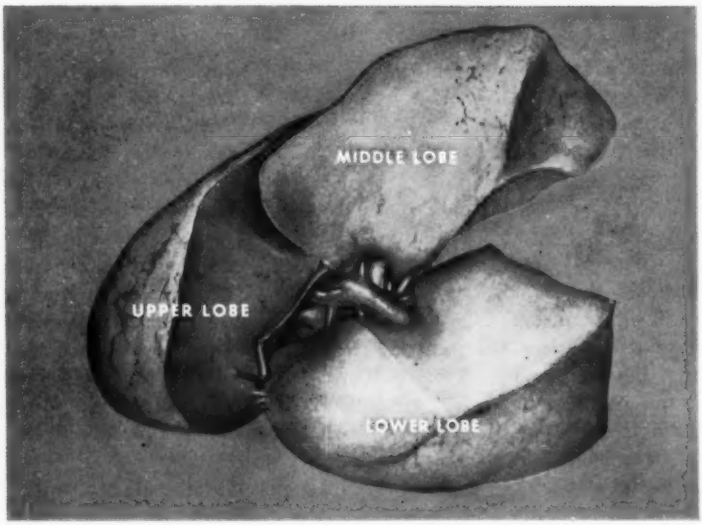


FIGURE 4.

FIGURE 3. A dissection of the interlobar portion of the right lung. The orientation is like that of figure 4, except that the middle lobe has not been elevated. Here, in blue, are shown those tributaries of the superior pulmonary vein which drain the segments of the upper and middle lobes; in red, are the branches of the right pulmonary artery which supply the segments of the lower lobe.

FIGURE 4. Interlobar fissures with the middle lobe elevated. This illustration is used to indicate where the arteries, veins and bronchi of the middle lobe may be found.

ACKNOWLEDGMENT

I am indebted to Pfizer Laboratories, Division, Chas. Pfizer & Co., Inc., for permission to reproduce these figures from the motion picture "Surgical Anatomy of the Pulmonary Hilum, Right Lung." This film was produced under a grant from Pfizer Laboratories and may be obtained on loan by writing to: Pfizer Laboratories, 630 Flushing Avenue, Brooklyn 6, New York.

Spontaneous Pneumothorax

J. BRADLEY AUST*

University of Minnesota Medical School, Minneapolis

SPONTANEOUS pneumothorax is a type of pneumothorax which occurs suddenly in an otherwise healthy person. Other types include traumatic, tuberculous and therapeutic or artificial pneumothorax.

Pathologic Physiology of Pneumothorax

Figure 1 depicts diagrammatically the chest wall, lung and pleural space. This is not a true space in life but only a potential space. A small bleb is shown in the diagram, and most persons, we hope, have few of these or none at all. There is atmospheric pressure outside and inside the lung. The arrows indicate the tension on the pleura due to the elasticity of the lung. The pleural space has a negative pressure because of this elasticity, and the measure of the pressure is a measure of the degree of elasticity of the lung. This varies between –2 and –14 cm. of water with respect to atmospheric pressure outside.

The pleural space reaches its maximal degree of negativity during inspiration. By closing the epiglottis one can, in a cough or sneeze, increase the intraalveolar pressure to 50 cm. of water, and this will also make the pleural pressure positive to an almost equal degree. A fair number of cases of pneumothorax occur under circumstances of exertion or stress when the epiglottis is closed and the person is making some intense effort, such as lifting a heavy object.

J. BRADLEY AUST

How does air get into the pleural space? It can enter from without or from within. Traumatic pneumothorax occurs when a missile enters the chest wall and creates an opening through which air can enter from the outside. Traumatic pneumothorax also can occur when a rib is fractured. The rib breaks, opens the parietal pleura and injures the visceral pleura, allowing air from the inside to fill the pleural space. The latter condition is a closed pneumothorax, in contrast to the former one which is called an open pneumothorax. Emphysematous blebs predispose to a break on the inside.

*Associate Professor, Department of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota.

Presented as part of a continuation course in Emergency Surgery for General Physicians, Center for Continuation Study, University of Minnesota Medical Center, Minneapolis.

Simple pneumothorax—Ordinarily, a small puncture wound through the chest wall or the rupture of a small bleb is self-controlled. Even a bullet wound may seal and produce only a partial pneumothorax. Similarly, when a bleb ruptures, the lung is pulled down and made more compact because of its elasticity and may close off the small opening which permitted the air to leave, and the result is a partial pneumothorax. This is a so-called simple pneumothorax. It is infrequently associated with any great degree of respiratory difficulty; the patient usually can walk around and can carry on some of his daily activities. He may be slightly dyspneic, and this dyspnea actually may be due to the pleural pain he has when he breathes deeply. Respiratory status is adequate for general activities, and there is no mediastinal shift.

Tension pneumothorax—Tension pneumothorax is produced when air enters the pleural space with inhalation and is prevented from escaping during exhalation by a valvelike action of an opening in the chest wall or lung. Because the air which enters cannot escape, tremendous pressure develops within the pleural space. This pressure forces the lung down, forces the mediastinum over to the opposite side, and impairs the filling of the heart with blood, producing very rapidly a situation of severe respiratory distress that can be lethal. A tension pneumothorax is an emergency situation and is simple to correct. Putting in a needle to allow air to flow both ways will solve the immediate problem; it will create a simple pneumothorax on the involved side but will take away the pressure on the other lung.

Spontaneous pneumothorax—Spontaneous pneumothorax is primarily a disease of healthy young men who presumably have congenital blebs on the surface of the lung. The usual cause is rupture of such an emphysematous bleb under stress, resulting in leakage of air into the pleural space.

Tuberculous pneumothorax—The breakdown of a caseous tuberculous focus near the periphery of the lung and its communication with a bronchiole produce a situation wherein air can enter the pleural space. In addition, if purulent material from the caseous nodule

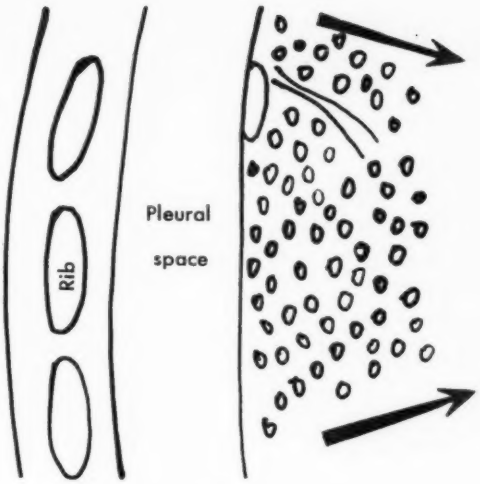


FIGURE 1.

can enter, the result is not only a pneumothorax but also a tuberculous empyema. It once was thought that this was the most common cause of spontaneous pneumothorax, and older textbooks contain the statement that a young person who has a spontaneous pneumothorax has tuberculosis. This is not true any longer. One sees tuberculous pneumothorax only rarely outside a sanatorium, and it is an ominous and often a terminal condition because of the associated tuberculous empyema.

Course and Treatment in 44 Cases of Spontaneous Pneumothorax

An examination of the records of the University of Minnesota's student health service for the past five years disclosed 44 cases of spontaneous pneumothorax. These patients represent a select group, the student health-service population. They ranged in age from 18 to 29 years. There are more men than women in the total school population, but the number of men in this group of 44 cases of pneumothorax seems disproportionately high.

Pain localized to the side of the pneumothorax was the primary presenting complaint in every case except one (table 1). The exception was a young woman in whom a 30 per cent pneumothorax was discovered on a routine chest x-ray. Only about half of the

TABLE 1

FINDINGS IN 44 PATIENTS WITH SPONTANEOUS PNEUMOTHORAX

FINDINGS	PATIENTS	
	Number	*Per cent*
Pain on side of pneumothorax	43	98
Dyspnea	21	48
Attack precipitated by exertion	17	39
Pleural effusion	10	23
Hemopneumothorax	1	2
Mediastinal shift	1	2
Blebs*	9	20

*Blebs were found at operation in two of the three patients who underwent pleurectomy.

TABLE 2

INCIDENCE OF RECURRENCE

INCIDENCE	PATIENTS	
	Number	*Per cent*
One or more documented recurrences*	15	34
More than two recurrences†	4	9

*There was a nondocumented history of recurrence in five additional cases. If these cases are included, almost half of the group (45 per cent) had more than one pneumothorax.

†These patients were advised to have a pleurectomy; three of the four patients underwent this procedure.

group had dyspnea; that is, when asked if they were short of breath, they said they were. None of them had severe dyspnea, even with 100 per cent collapse.

Exertion precipitated the attack in about 40 per cent and ranged from a cough or sneeze to blowing a trumpet, getting out of bed, lifting a davenport, or playing tennis.

Pleural effusion is not a major consequence of simple pneumothorax. Twenty-three per cent of the patients had pleural effusion, but it was minimal in amount except in one case. The irritating effect of the air in the pleural space causes a certain amount of extra secretion. In the average case it would not be detectable on an x-ray, because it is said that 100 to 200 cc. must be present before detection is possible.

One patient had a massive hemopneumothorax. This can happen if the bleb is in a region where it will rupture a blood vessel when it breaks. In the one case of massive hemopneumothorax, 1000 cc. of blood was removed.

In only one case of spontaneous pneumothorax was a mediastinal shift found.

We could demonstrate blebs or questionable blebs in the x-rays in nine of the 44 cases (20 per cent). These blebs often are difficult to visualize roentgenographically. We would postulate that they are present in all the cases of spontaneous pneumothorax, but we cannot find them in every instance. In two of the

TABLE 3

TREATMENT IN 39 CASES

	NO TREATMENT	BED REST	TUBE ASPIRATION THERAPY
Number of patients	8	25	6
Days hospitalized	—	2-11	2-13
Average	—	6.5	6.5
Days required for re-expansion	7-60	4-56	1-5
Average	21	16	2
Extent of pneumothorax (per cent)	5-35	5-100	15-100
Average (per cent)	16	28	54

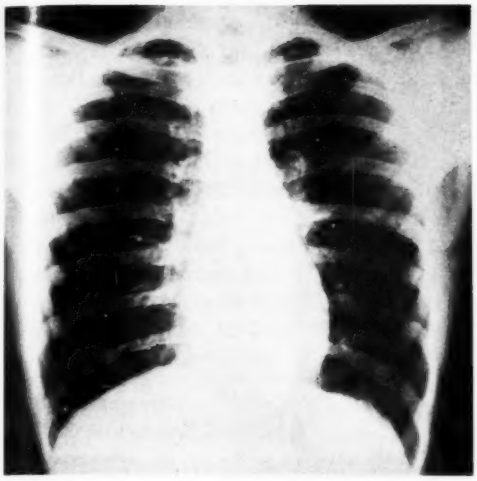


FIGURE 2.

FIGURE 3.

three patients who underwent pleurectomy, blebs were found at operation and removed.

Table 2 shows the incidence of documented recurrences. Thirty-four per cent of the patients had one or more recurrences of pneumothorax. In five additional cases there was a history of similar episodes but the patients did not consult a doctor or an x-ray was not made. If we include the latter cases, almost half of the group had more than one pneumothorax. Only four (9 per cent) had more than two recurrences. All four were advised to have pleurectomy. Three of the four took the advice.

The results of treatment are shown in table 3. Eight patients had no treatment; that is, they were seen in the health service and went home, without being hospitalized. Follow-up roentgenograms in these eight cases show that it took between 7 and 60 days (average 21 days) for re-expansion to occur. The extent of the pneumothorax in these eight cases averaged 16 per cent.

Twenty-five patients were hospitalized and treated by bed rest. The average stay in the hospital was six and one-half days. From 4 to 56 days (average 16 days) were required for re-expansion. Notice that the average period required for re-expansion was longer without treatment than with bed rest. The extent of the pneumothorax in the hospitalized group was somewhat greater, and ranged up to 100 per cent.

Tube aspiration therapy was used in only six cases, all in the last three years. Up to three years ago (in the first two years of the period covered in this survey), patients were seen on the medical service only, without surgical consultation. When the surgeon was consulted, more patients were treated by tube aspiration.

The average hospital stay for the six patients who had tube aspiration therapy was six and one-half days, the same as the average for the 25 patients treated by bed rest. But complete expansion required between one and five days (average two days) in spite of the fact that the pneumothorax usually was twice as severe as in the afore-mentioned 25 cases.

Four of the 44 patients had 100 per cent collapse, which means that the lung was contracted to its minimal volume. Two were treated by bed rest. They were hospitalized for seven days and six days, respectively, and re-expansion required 31 days and 56 days. The other two patients with 100 per cent collapse were treated by tube. They were hospitalized two days and five days, respectively, and re-expansion required one day and four days.

The contrast between these two types of treatment in regard to the time required for

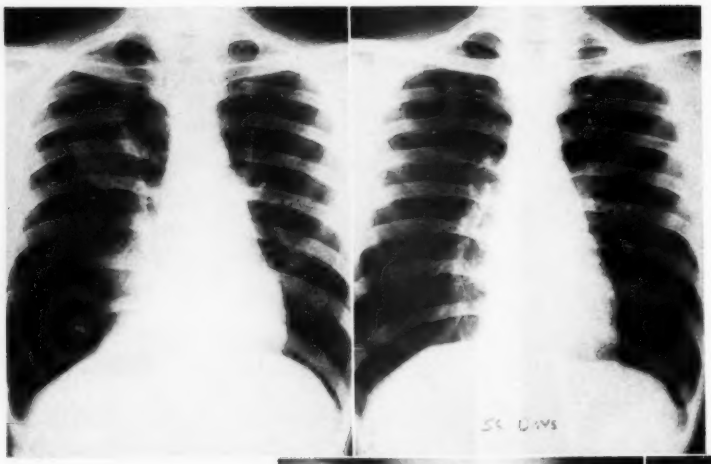


FIGURE 4.

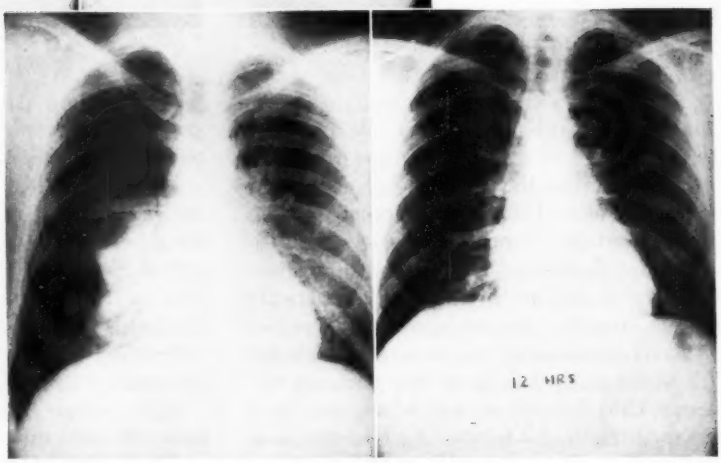


FIGURE 5.

re-expansion is obvious. However, as you know, many persons who have had artificial pneumothorax have gone along for years without a great deal of difficulty, and little concern has been shown about leaving a simple pneumothorax untreated. I would like to take issue with that view. Figure 2 represents a situation which I think argues against it. The patient, a young man, has a very small pneumothorax, which has been re-expanding; it was worse. But notice that on the opposite side a cluster of blebs is visible. This is a potentially dangerous situation, because while one-sided pneumothorax is readily tolerated, bilateral pneumothorax is universally fatal. If this young man had a full collapse on one side and re-expansion were permitted to take as long as 56 days, the blebs on the opposite side could rupture and he would be in serious trouble. Only one of our patients had a history of bilateral pneumothorax; pleurectomy subsequently was performed on one side.

Figure 3 represents the patient who had hemopneumothorax; 1000 cc. of bloody fluid was removed. This situation is always an indication for tube therapy. If tube therapy is not employed, there is a good chance that the blood will compress the lung; then a peel of thick pleura will form, the lung will not re-expand normally, and a decortication will be necessary at a later date.

Figures 4 and 5 represent two of the cases

of 100 per cent collapse. In figure 4 you will notice that although this is called a 100 per cent collapse there is an adhesion holding the upper lobe out against the chest wall; but the rest of the lung is completely collapsed. This patient was hospitalized for six days and then released, and it took 56 days for re-expansion to occur; a film taken after 49 days still showed a 15 per cent pneumothorax. In contrast, figure 5 represents a patient with 100 per cent pneumothorax who received tube aspiration therapy for 12 hours. The lung is re-expanded and has remained expanded.

Tube Aspiration Therapy; Indications and Methods

In the past, most cases of pneumothorax have been treated by watching, bed rest, and routine x-ray follow-up to make sure re-expansion was proceeding. The survey of 44 cases that I have summarized suggests it would be much safer, and patients probably could resume their usual activity sooner, if aspiration therapy were carried out in all instances in which more than 20 per cent of the lung is collapsed. The other obvious indications for tube aspiration therapy are severe dyspnea, mediastinal shift, tension pneumothorax and severe pleural effusion (which may well be a hemopneumothorax).

A number of tubing methods may be employed, and the one used will vary from physician to physician. A No. 15 needle can be used, and a polyethylene tube inserted through its lumen and connected to a suction device, or, after manual aspiration, to water-seal drainage. If this therapy is continued for 24 hours and if an x-ray made two or three hours after clamping the tube shows that the lung is still expanded, it is safe to pull out the tube. Some physicians prefer a larger-bore rubber tube connected to suction, and this also works quite satisfactorily. With tube aspiration therapy, the patient must be kept in bed for at least 24 to 48 hours and one must watch him for a day or two afterward to make sure the lung is going to stay expanded. However, I think it is a more satisfactory solution to the problem than merely following a 100 per cent collapse roentgenographically.

Treatment of Recurrent Pneumothorax

The objective of treatment for recurrent pneumothorax is to obliterate the pleural space so that it is no longer a potential space by provoking adhesions between the visceral and parietal pleurae. To this end, everything from talc to hypertonic solutions has been put into the pleural space in the hope of creating sufficient reaction to obliterate the space. Surgically we have found that the most satisfactory procedure in our hands is removal of the parietal pleura from the chest wall. The pleura overlying the diaphragm and the mediastinum need not be removed. Removing the parietal pleura is a relatively simple procedure. Pleurectomy is a very efficient way of handling the problem. However, I think one should not resort to it unless there is good evidence that the patient has had pneumothorax on more than two occasions.

Discussion

QUESTION: You mentioned a polyethylene tube in connection with suction. Do you mean nasal suction?

DR. AUST: No. Suction should be of a very light character, that is, not more than 20 cm. of water. Any suction apparatus that can be regulated to produce a negative pressure that low would be satisfactory. Most physicians use a water seal; in other words, they aspirate the lung at the time they put in the tube, and then just put the tube under water. This will suffice as long as the patient is able to breathe and empty that space. But suction provides more control over subsequent air leakage.

QUESTION: What interspace do you usually enter when you put in the tube?

DR. AUST: It depends on what the patient is going to do afterward. If he is going to be at rest in bed, I usually insert the tube in the highest point in the thorax at the second interspace anteriorly. If he is going to be sitting up, one can still use a high space if the purpose is to aspirate air, but if the patient has a hemopneumothorax and the object is to drain fluid, I insert the tube in the ninth interspace at the midaxillary line.

Traumatic Hemopneumothorax

SAMUEL W. HUNTER*

University of Minnesota Medical School, Minneapolis

SAMUEL W. HUNTER

If Michelangelo had fallen from the roof of the Sistine Chapel in the sixteenth century, he might have sustained a hemopneumothorax. Pope Julius II's physicians would have attempted a cure. If the surgeon who saw him first was the one who held that the crushed chest should remain open to allow the bad humors to exit, the chest would have been allowed to remain open or it may even have been opened surgically. On the other hand, a second surgeon in service to the Pope might have insisted on closing the chest wall to seal in the "good" humors.

Today, some 450 years later, we know that an open hemopneumothorax should be converted to the closed type, but the divergence of opinion on the ensuing problems is almost as wide as it was then.

*Assistant Professor, Department of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota.

Presented as part of a continuation course in Emergency Surgery for General Physicians, Center for Continuation Study, University of Minnesota Medical Center, Minneapolis.

The vast majority of traumatic thoracic injuries are the direct result of our bigger and faster cars plus the inability of drivers to resist using this power for their own and others' destruction. The Indiana Highway Commission reported in 1959 that 25 per cent of the highway deaths in that state were due directly to thoracic trauma.

Other types of trauma may produce hemopneumothorax, such as penetrating wounds by bullets or ice picks, falls, endoscopy and surgery. When the patient is seen in the accident ward, varying stages of anoxia and shock will be evident. Although other problems may complicate the picture, such as neurologic or abdominal injuries, the chest problem must be handled first.

Open Hemopneumothorax

The air in the pleural cavity must come from either within or without. Let us consider open hemopneumothorax first. If the chest wall is smashed like an eggshell, the atmospheric pressure rushes in quickly to deflate the lung. This is seen very readily during a surgical procedure when the chest is opened, particularly when the anesthesiologist chooses not to apply positive pressure. A patient with this type of injury must receive help in a

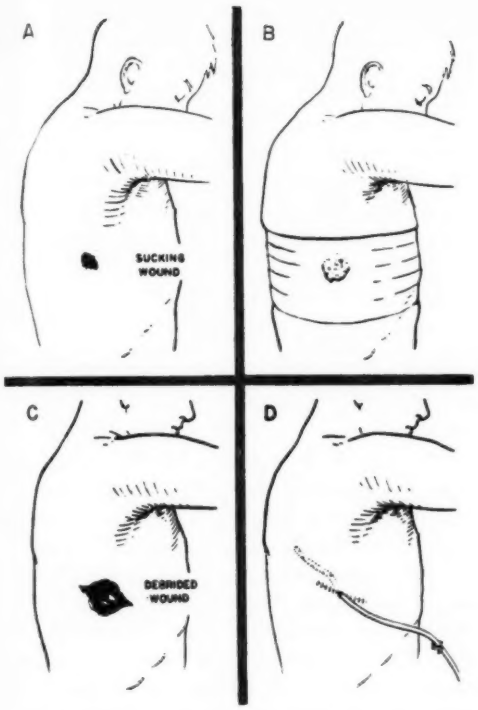


FIGURE 1. Sucking wound of the chest, and closure with large, heavy compression dressing. Debridement should be done quickly if possible. Tubes are placed in the chest to remove fluid and air.

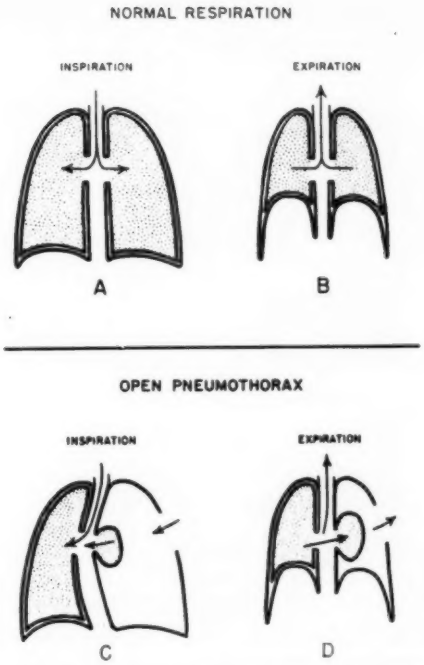


FIGURE 2. In open pneumothorax, the atmospheric pressure deflates the lung. On inspiration, fresh air passes into the good lung but stale air rushes over from the deflated lung. On expiration, air is forced into the deflated lung and also out the trachea; therefore, the dead space is increased.

Figures 1 and 2 from Kirby, C. K. and Johnson, J.: Surgery of the Chest. Chicago, The Year Book Publishers, Inc., 1958.

hurry. The lung is deflated; there is air hunger, and a torn intercostal artery may have caused considerable loss of blood. The external hemopneumothorax must be converted to a closed one immediately. A tube or tubes must be placed in the thoracic cavity to remove air and blood.

Figure 1A illustrates a sucking wound of the chest. The loud sucking wound plus the patient's struggle for air make the diagnosis self-evident. Also shown, in figure 1B, is the closure of the wound with a large, heavy compression dressing. Debridement should be done quickly if possible (figure 1C). A chest tube is placed either through the wound or through an extra opening in the chest wall posteriorly to remove fluid (blood). To remove air, a second tube should be placed in the anterior chest wall. If multiple ribs or the sternum or both are fractured, some type of stabilization of the chest will be necessary. Simple measures are effective, such as sandbagging a flail chest wall or splinting with strips of orange crate or a towel clip in the sternum attached to traction.

The patient will attempt to compensate for anoxia by breathing more rapidly. He is unable to breathe deeply because of anxiety and severe pain. The more rapidly he breathes, the more inefficiently he breathes. Notice in the drawings depicting open hemopneumothorax in figure 2 that the atmospheric pressure deflates the lung. Fresh air passes through the trachea into the good lung, but "used-up" or stale air rushes over from the deflated lung. On expiration, air is forced into the deflated lung and also out the trachea. This causes an

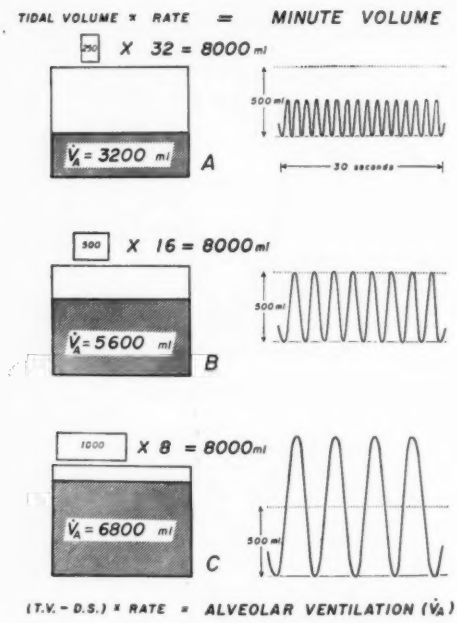


FIGURE 3. Effect of changes in tidal volume and frequency on alveolar ventilation/minute.

increase in the dead space at a most inopportune time.

As already stated, the patient breathes more rapidly to compensate for anoxia, but the exchange may be ineffective. Oxygenation and carbon dioxide loss are directly proportional to alveolar ventilation. Alveolar ventilation is calculated by subtracting the dead space from the tidal volume and multiplying the result by the respiratory rate. In figure 3, notice in the top bracket that the patient's tidal volume is 250 cc. Alveolar ventilation (tidal volume minus dead space times respiratory rate) is 3200, which is just borderline (dead space is 150 cc.). That patient is going to be anoxic even though the minute volume is 8000 cc. The dead space is increased beyond 150 cc. by the "stale air-breathing effect" (paradoxical or pendular-type respiration).

Figure 4 depicts this situation even more dramatically, showing again that tidal volume minus dead space times the respiratory rate equals alveolar ventilation. The patient represented on the left side of the diagram might well be one who has an open pneumothorax or a crushed chest. He is moving only enough air to shuttle back and forth the dead-space air into the lungs. It is obvious that this patient will survive only if something is done so that the dead space can be decreased from 150 to 80 cc. and the secretions can be handled more readily. This something is, of course, tracheostomy, a most important step for the severe cases.

Hemopneumothorax of the open type, therefore, must be converted quickly to the closed type. Bleeding must be controlled. To hope that the re-expansion of the lung will tamponade a large torn systemic vessel is wishful thinking. If a large vessel in the chest wall is cut, it should be exposed in the operating room or emergency ward and ligated directly.

It is alarming how drastic a decrease in oxygenation occurs with minimal contusion of a lung. Figure 5 represents work by Jensen and Miller at the Minneapolis Veterans Administration Hospital. Notice that the good lung (this is a patient who had only a very minor blow to the chest) has an oxygen uptake of 75 per cent, and the injured lung only a 25 per cent uptake. If this is true for a patient who sustained only a moderate thump on the chest wall, one can imagine how much the oxygen uptake decreases when there is severe contusion of the lung.

Assuming that emergency thoracotomy becomes necessary (and I do not mean to imply that it does in the majority of cases), the bleeding point or points should be ligated, the lung re-expanded, any bits of foreign material removed, the tubes placed, and the chest wall closed. Tracheostomy is performed either after or, more likely, before thoracotomy. The patient is then treated by careful suction of the tracheobronchial tree, administration of oxygen (humidified) and antibiotics, and judicious use of pain-relieving agents.

It is the unusual case in which a chest tube will evacuate all the blood in a hemothorax, but a small amount of blood in the thoracic space can be tolerated. Some surgeons, particularly Dr. Rowe in California, prefer to evacuate all the blood immediately. Dr. Rowe operates very early. I personally prefer to

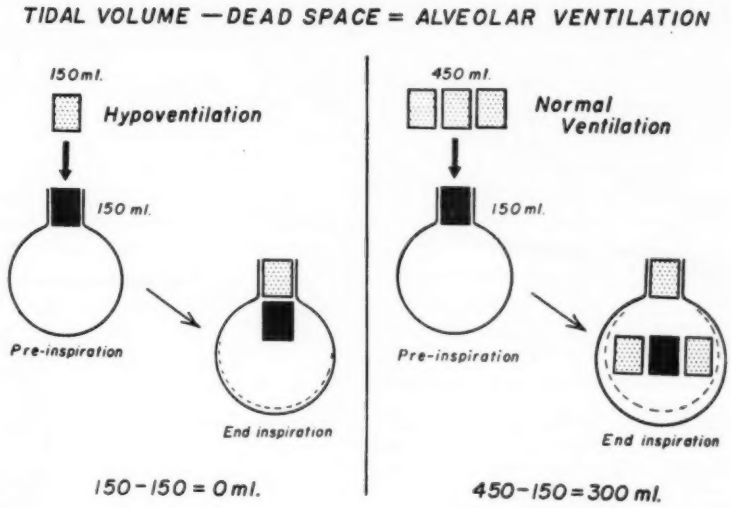


FIGURE 4. Relation of the tidal volume, the anatomic dead space, and the alveolar ventilation.

Figures 3 and 4 from Comroe, J. H., Jr.: The Lung. Chicago, The Year Book Publishers, Inc., 1955.

evacuate all the blood possible by the tube method, and delay the decortication for a few or several weeks. I would not hesitate to operate earlier, however, if the space occupied by the blood were increasing, if respiratory embarrassment resulted from the compressive effect of the hemothorax on the lung, or if there were evidence that infection was present.

Although in my estimation tube drainage is preferable, many writers maintain that needle thoracentesis can be used successfully. In a recently reported series it was demonstrated that needle thoracentesis, if it is performed successfully and repeatedly, will result in a good re-expansion of the lung and control of the blood in the thoracic cavity. I would rather place the tube and drain as much blood as possible and then use the needle aspiration for spot treatment—in other words, use the needle technic in the areas where the tube is not handling the situation.

Closed Hemopneumothorax

The closed type of hemopneumothorax is possibly less dramatic than the open type but is more insidious. The air may come from a contused lung or literally "popped-out" lung tissue. It may also come from a torn bronchus or even the trachea. In a dramatic case reported recently in the *Journal of Thoracic Surgery*, a patient's trachea was transected in an automobile accident. The patient survived only because the surgeon recognized the problem immediately, cut down on the cervical trachea, repaired it, and did a tracheostomy.

The air must come from the lungs themselves, from torn bronchi, from the trachea, or from another source in the thoracic cavity which is sometimes overlooked—the esophagus. If the esophagus is torn, thoracotomy should be performed and the leak closed. Blood may come from the same area of violence as the air, but it is surprising how few cases we see in which both blood and air are present; usually it is only air. If a peripheral pulmonary vessel is torn, it may seal off and the bleeding may stop, so that nothing further need be done except tube drainage. If the blood comes from a major pulmonary artery or vein, however, the possibility of stopping the flow by re-expansion of the lung is quite slim. These patients, of course, may never reach the accident ward.

Figure 6 illustrates a closed pneumothorax. The patient also has subcutaneous emphysema, which is more troublesome to the doctor and the patient's relatives than it is to the patient —unless, of course, subcutaneous air compresses the trachea. The air will recede in a few days as it is picked up by the venous circulation.

A patient who has a badly contused lung

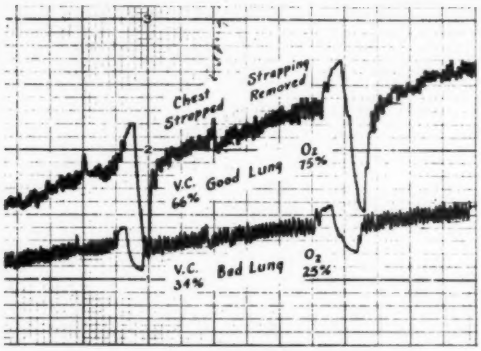


FIGURE 5. Differential bronchospirometric tracings of young male with minor crushing injury of chest, only one rib fractured. Note that tidal air and minute volume are the same on both sides, but vital capacity and oxygen uptake are greatly diminished on injured side. Chest strapping has no effect on normal exchange where only one side is injured and is not flail.

From Jensen, N. K.: Recovery of pulmonary function after crushing injuries of the chest. Dis. Chest 22:319 (September) 1952.

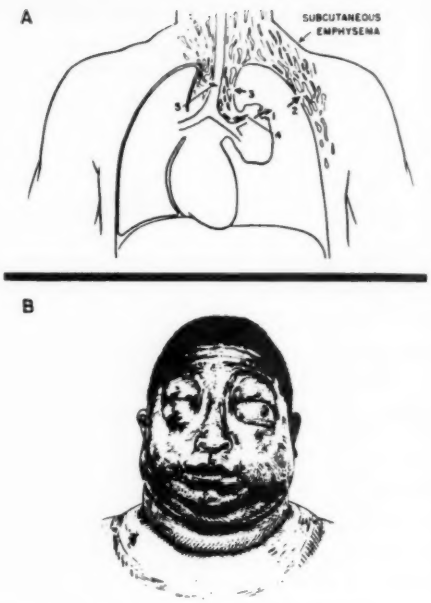


FIGURE 6. Closed pneumothorax. The patient also has subcutaneous emphysema.

From Kirby, C. K. and Johnson, J.: Surgery of the Chest. Chicago, The Year Book Publishers, Inc., 1958.

may or may not have severe respiratory and circulatory distress. Actually, such a situation in a healthy young person may be missed in the accident ward. The severe type, however, usually is recognized at once. This is one of the very few excuses for the speeding ambulance. When such a patient reaches the accident ward, there is no time for an x-ray. The patient is anxious, ashen, uncooperative, sweaty and struggling for air. The intern must act quickly and accurately without the help of an x-ray. He listens with the stethoscope and finds that the lung on the affected side is not moving. Immediately he should insert a large needle in the anterior chest wall and suck out as much air as possible. If the patient's color improves, a few moments may be spared to make a chest x-ray with a portable machine. If improvement is not obvious, aspiration should be repeated, or a tube inserted anteriorly for removal of air and a posterior tube placed if bleeding is suspected.

Other measures can be taken care of quickly. Tracheostomy should be done, of course, if an airway problem persists. Blood transfusions should be given to replace loss, oxygen should be administered, and pain relieved.

If blood loss is excessive (and I think 1500 or 2000 cc. is excessive), the operating-room staff should be alerted. If leakage of air is excessive (so that with two size 24 catheters in the chest one cannot keep up with the loss), it is logical to assume a large bronchus is torn or ripped. To attempt expansion of the lung with one or two tubes in such a situation is useless. Again, the patient must be taken to the operating room, the torn bronchus must be repaired, and the bleeding stopped.

If the subdiaphragmatic contents are involved in the injury (such as the liver, stomach or intestines), the incidence of infected hemothorax is increased. The hazard of prolonged closed or conservative therapy is increased, so that this situation predicates the open or operative type of treatment.

There are five definite indications for immediate thoracotomy: (1) uncontrolled intrapleural hemorrhage, (2) uncontrolled leakage of air due to a tear in the trachea or larger bronchi, (3) wounds of the mediastinal organs, (4) wounds involving the diaphragm

and the viscera, and (5) large foreign bodies within the pleural cavity.

Presuming that active bleeding has ceased, an untreated hemothorax shows, at first, an increase in volume. Why? Because the blood is autolyzing and the large molecules are being changed to smaller but more numerous molecules, increasing the osmotic tension of the fluid within the cavity, attracting more fluid, and increasing the size of the hemothorax. The change may not be easily detectable by x-ray examination.

Occasionally the blood of a hemothorax fails to clot, but more commonly it clots. If it clots, it undergoes organization. In the early stages this process is incomplete and a peripheral membrane surrounds the clotted material. Gradually the red blood cells are destroyed. When one operates on these patients one finds a capsule almost like a football bladder, and inside this capsule, which is compressing the lung, material that resembles stringy chocolate milk (red cells which have gradually been destroyed and partially removed). This peel can be stripped off at various stages from the chest wall. From the parietal pleura the peel may be stripped off through the endothoracic fascia. I have found this method to be rather bloody. I prefer to develop a plane between the peel and the parietal pleura, leaving the parietal pleura intact on the chest wall. From the visceral surface of the lung, the operation is easier if the procedure is carried out at about four to six weeks. This operation must be performed for clotted hemofibrothorax. If not, over a period of six or seven weeks the lung is pushed against the mediastinum and becomes useless.

In regard to chemical debridement, I have little to say. I have used it four or five times, have had little success, and do not like it.

Summary

Open hemopneumothorax must be converted to a closed type. Tube aspiration is carried out anteriorly and posteriorly. Nothing further need be done for the emergency if the patient is getting enough oxygen and the bleeding is staunched. Thoracotomy is necessary if these measures fail to control the hemothorax or pneumothorax. Tracheostomy is a great boon; it will serve to decrease the dead space and facilitate handling of troublesome secretions. Humidified oxygen and blood replacement also may be necessary.

In closed hemopneumothorax the same measures are applicable, although the diagnosis may be less obvious.

Fourth Annual Awards for Medical Writing

The fourth annual competition for unpublished manuscripts on clinical subjects in the field of internal medicine has been announced by the editors of the Modern Medical Monographs series. The purpose of these awards is to stimulate young physicians to achieve high standards of medical writing in the classic monograph form. First prize is $500. In addition, authors whose manuscripts are found suitable will be offered publication contracts for books in the Modern Medical Monographs series. Information on contest rules and manuscript requirements is available from Dr. Irving S. Wright, 450 East 69th Street, New York 21.

Tracheostomy in Traumatic Injuries

YOSHIO SAKO*

University of Minnesota Medical School, Minneapolis

THE importance of tracheostomy in patients with severe chest injuries is well recognized, but this recognition has come about only in recent years.

YOSHIO SAKO

In World War II casualties, Brewer and associates[1] observed that resuscitation of the injured was difficult when fluid accumulated in the lower respiratory tract. Accumulation of fluid occurred in those with injuries of the abdomen, head, and especially the chest. Intercostal nerve block, catheter and bronchoscopic aspiration, positive pressure oxygen, and stabilization of the flail chest were effective in managing the "wet lung" resulting from severe chest injury.

Baronofsky, Dickman and Vanderhoof[2] were among the earliest to recommend tracheostomy in the management of a patient with a flail chest and a wet lung resulting from trauma. The profuse bronchial secretion in this patient could be removed satisfactorily only after a tracheostomy was performed.

Carter and Giuseffi[3] were the first to report on a series of cases in which tracheostomy was performed routinely for the management of patients with crushed chests. Since the appearance of their report, tracheostomy has become widely recognized as an essential maneuver, along with other procedures such as correction of pneumothorax and hemothorax, stabilization of the flail chest, and intercostal nerve block, for managing a severe chest injury.

Effects of Tracheostomy

The most obvious beneficial effect of a tracheostomy in a patient who has a crushed chest and fluid accumulation in the tracheobronchial tree, in one who is conscious and especially in one who is unconscious, is the ease with which tracheobronchial secretions can be removed repeatedly. Numerous factors contribute to the formation of fluid in the lower respiratory tract in the patient with chest injury. These are pulmonary parenchymal injury, anoxia, increased respiratory effort, bronchospasm, and tracheal obstruction. Pain results in splinting of the chest, inhibition of cough, and short, rapid breathing, all favoring fluid accumulation and retention.

Carter and Giuseffi were the first to empha-

*Associate Professor, Department of Surgery, University of Minnesota Medical School, and Veterans Administration Hospital, Minneapolis, Minnesota.

Presented as part of a continuation course in Emergency Surgery for General Physicians, Center for Continuation Study, University of Minnesota Medical Center, Minneapolis.

size the beneficial effects of tracheostomy on the mechanics of ventilation. These include a decrease in respiratory dead space and a decrease in resistance to air flow during the respiratory cycle. Decrease in dead space is essential in an injured patient whose breathing is rapid and shallow. His tidal air is subnormal, but a tracheostomy would eliminate about 100 cc. of dead space; thus, with the same rate and depth of breathing, ventilation would be increased by 100 cc. for each respiratory cycle.

Tracheostomy reduces the resistance to air flow, because the narrow area in the larynx as well as the normal resistance offered by the upper air passages are bypassed. Edema, spasm and accumulation of secretions would also add to the resistance to air flow normally present. Decrease in resistance to air passage is particularly beneficial to the patient who has an unstable chest wall resulting from multiple rib fractures. Since less effort is required to move the same volume of air, the degree of movement of the injured parts will be reduced, with corresponding reduction in pain and paradoxical respiratory movements.

Technic of Tracheostomy

Although tracheostomy is a minor operation, the procedure may at times be very difficult with an uncooperative patient or a patient with a short, thick neck, or because of the urgency of the situation or lack of assistance and adequate lighting. Whenever possible the tracheostomy should be performed in the operating room and as an elective procedure. This implies that the need for a tracheostomy should be considered early and that the operation should be performed before the situation becomes desperate. Seemingly minor details such as proper positioning, lighting, and the availability of a suction apparatus are in reality very important for simplifying the procedure.

Proper positioning consists of having the shoulder and neck supported by a firm support such as a sand bag so that the head is well extended and the neck is stretched. Procaine infiltration anesthesia is used, and a vertical midline incision from just below the thyroid cartilage to the suprasternal notch is made through the skin, subcutaneous tissue and the anterior cervical fascia. The sternohyoid and sternothyroid muscles are retracted laterally and the incision is deepened until the fascia covering the trachea is exposed. The thyroid isthmus may be retracted inferiorly or superiorly or divided in order to expose the second, third and fourth tracheal rings. Before the tracheal rings are incised, the tracheostomy tube should be checked and be available for immediate insertion. The suction tip should be in the wound to clear away any blood that might enter the trachea. The second and third cartilaginous rings are incised, removing an oval ring from the tracheal wall to accommodate the tracheostomy tube. The oval piece of tissue should be securely grasped to prevent aspiration of the tissue. In children marked flexibility of the tracheal rings permits insertion of the tube without removal of a piece of the tracheal wall. The largest-sized tube that can be accommodated by the trachea is introduced.

After the tracheostomy tube is placed and secured, the wound may be examined for complete hemostasis. The wound is then closed rather loosely with catgut to the subcutaneous tissues and the skin closed loosely with silk. In a thin person with a small incision, frequently no wound closure is needed.

The value of a tracheostomy will long be remembered if one is exposed to just one patient with a crushed chest who is cyanotic, gurgling, struggling, apprehensive and hypotensive, and who has rapid, shallow breathing and progressive subcutaneous emphysema. As soon as the tracheostomy is done, fluid, froth and mucus are coughed out faster than one is able to suction him; he ceases to struggle, color improves, blood pressure begins to rise, respirations become deeper and calmer, and frequently the patient begins to doze.

Precautions During Tracheostomy

Accidents will be avoided if the incision is made in the midline and the cricoid cartilage is held between the forefinger and thumb of the left hand as the incision is made and until the trachea is exposed. This maneuver is es-

sential when one is operating on a patient with a thick neck or on one who has marked subcutaneous emphysema. Slight deviations from the midline may not be apparent in such a patient. Bleeding will be greater when the incision deviates from the midline. The fascia overlying the tracheal ring is divided until the shiny rings of the trachea are exposed. If an assistant retracts superiorly on the trachea with a sharp hook around the cricoid cartilage, the trachea may be brought into clearer view. Inadequate exposure and visualization of the tracheal rings by division of the pretracheal fascia may result in false passage of the tracheostomy tube between the fascia and trachea or between the trachea and lateral structures into the superior mediastinum.

In children, deviation from the midline increases the likelihood of creating a pneumothorax because of a relatively high position of the apical pleural reflection. Care must be taken when the trachea is incised that the knife is not plunged too deeply, lest the posterior tracheal wall and anterior esophageal wall be pierced. This may occur if the patient should cough violently at the time that the trachea is incised. If 1 to 2 cc. of a topical anesthetic agent is injected into the trachea a few moments before the trachea is incised, the coughing and straining may be eliminated.

Tracheostomy Aftercare

The nasopharyngeal passages normally warm and humidify the air before it reaches the lower respiratory tract. Bypassing the "air conditioning" function of the nasopharynx with a tracheostomy causes varying degrees of tracheitis. Incrustations will form in the tracheostomy tube and in the trachea and frequent cleansing of the tube is necessary. For the first two to three days only the inner cannula of the tube is changed, because the tracheostomy site will not be healed sufficiently to form a secure tract and replacement of the tube may be difficult. Thereafter the entire tube should be changed daily. Humidified air should be directed toward the tracheostomy tube or the entire room should be humidified for maximal comfort. A cuffed tracheostomy tube may be employed if positive pressure insufflation is to be used with any one of the automatic or semiautomatic respirators available today. In the average patient with a severe chest injury, a tracheostomy may be needed for 10 to 14 days. In an unconscious patient the tracheostomy may be needed for a longer period. As the time approaches for removal of the tube, a smaller-sized tube may be inserted and the external opening closed with a cork to see if the patient would tolerate removal of the tube.

Conclusion

In patients with severe chest injuries, resuscitation requires correction of numerous derangements such as blood loss, hemopneumothorax, unstable chest wall, relief from pain, and treatment of injuries elsewhere in the body. In spite of attention to these points, the patient may do poorly because of fluid accumulation in the tracheobronchial tree and borderline anoxia. An early tracheostomy will permit cleansing of the tracheobronchial tree and prevent the patient from "drowning in his own secretions." Reduction in respiratory dead space by tracheostomy leads to utilization of a larger proportion of the tidal air for effective ventilation. Shortening of the air passage and bypassing the larynx and nasopharynx reduce resistance to air flow, and less effort is required to move a given volume of air. Decrease in respiratory effort leads to reduction in pain and diminution of paradoxical movement of unstable portions of the chest wall. Even when the patient appears to be *in extremis*, a tracheostomy will often produce a dramatic favorable response by breaking the cycle of excessive tracheobronchial secretion and anoxia.

REFERENCES

1. Brewer, L. A., Burbank, B., Samson, P. C. and Schiff, C. A.: The "wet lung" in war casualties. Ann. Surg. 123:343-362, 1946.
2. Baronofsky, I. D., Dickman, R. W. and Vanderhoof, E. S.: The treatment of acute chest injuries with especial reference to the use of tracheotomy. Minnesota Med. 33:49-53, 1950.
3. Carter, B. N. and Giuseffi, J.: Tracheotomy, a useful procedure in thoracic surgery, with particular reference to its employment in crushing injuries of the thorax. J. Thoracic Surg. 21:495-505, 1951.

Traumatic Rupture of the Diaphragm

LLOYD D. MacLEAN*

University of Minnesota Medical School, Minneapolis

TRAUMATIC rupture of the diaphragm usually is the result of a severe crushing injury. Our experience indicates that it occurs predominantly in automobile accidents—and in persons who have had considerably more than "one for the road."

LLOYD D. MACLEAN

I will review 26 cases of traumatic rupture of the diaphragm which were seen at the University of Minnesota Hospitals, Minneapolis, and at the Ancker Hospital, St. Paul, over an 18 year period, from 1940 through 1958. The patients at Ancker Hospital were almost all seen immediately after the injury, whereas many of those at the University Hospitals were seen at various periods of time afterward, up to 10 years. Thus, this group shows the long-range effects of the injury as well as the crucial initial problem.

*Assistant Professor, Department of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota.

Presented as part of a continuation course in Emergency Surgery for General Physicians, Center for Continuation Study, University of Minnesota Medical Center, Minneapolis.

The incidence of traumatic rupture of the diaphragm apparently is increasing. Three-fourths of the injuries in these 26 patients occurred after 1952, and one-third of the patients were seen in the last year of the study, 1958. At one time at Ancker Hospital there were three cases of traumatic rupture of the diaphragm on the surgical service all at once.

The best description of traumatic rupture of the diaphragm that I have read was presented in the *Buffalo Medical Journal* in 1853 by Henry I. Bowditch. Bowditch was the first man in this country, probably in the world, to make the diagnosis ante mortem, although Ambroise Paré had recognized the condition post mortem in the sixteenth century. Bowditch used five clinical signs that are still extremely useful: (1) prominence and immobility of the left side of the chest (most of these injuries involve the left side), (2) absence of breath sounds on that side, (3) bowel sounds on that side, (4) shifting of the heart to the right, and (5) tympanites of the left side of the chest to percussion. The last-named finding is completely opposite from what one would expect from the appearance of the chest roentgenogram. If one bears in mind

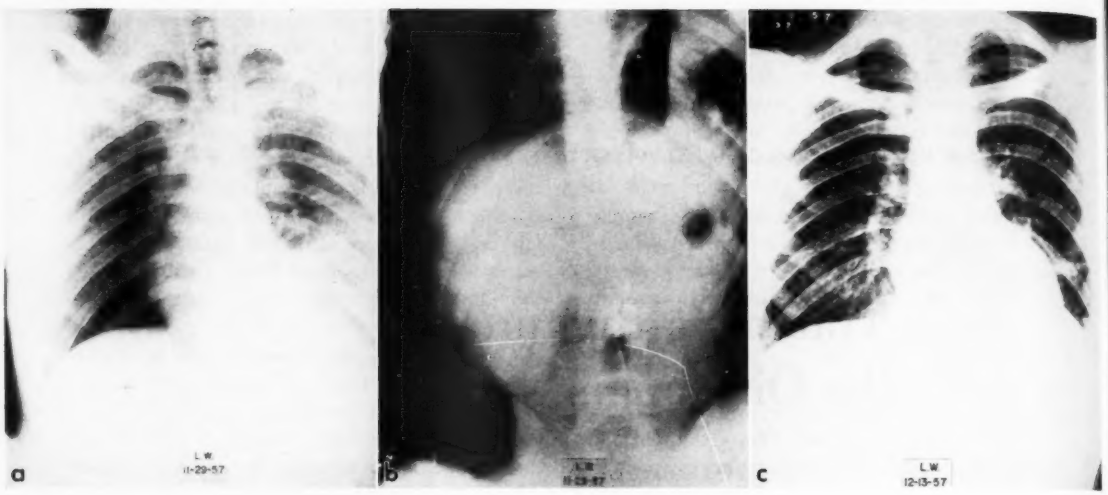


FIGURE 1. Case 1.

a. "Elevation of left diaphragm" with smooth contour characteristically seen after a traumatic rupture.

b. Lateral decubitus film reveals an air-fluid level in viscus in the left side of the chest that was not obvious on the posteroanterior roentgenogram.

c. Postoperative chest film. Normal location of repaired left diaphragm.

these signs and studies the x-ray, one is astonished to find that the left side of the chest is completely opacified and is tympanitic on percussion—the inference being that there is a hollow viscus inside which is not at all obvious on the plain chest x-ray.

Bowditch studied this problem extensively, going back over all the postmortem reports that had been made since 1573 when Paré first described two patients with traumatic rupture of the diaphragm. He recognized that a patient could survive the injury which caused the diaphragmatic rupture, that the rupture could go unrecognized, and that months or years later he would be stricken with the complications. I firmly believe that every patient who has a traumatic rupture of the diaphragm will get a complication from it.

One of Paré's patients died eight months after extensive trauma which almost certainly caused the rupture of the diaphragm. The postmortem examination disclosed a ruptured diaphragm with strangulated bowel in the thoracic cavity.

Even before 1853, it was suggested that traumatic diaphragmatic rupture could be repaired surgically, and a few attempts at repair were made before the turn of the century. However, I think the first successful repair was made in 1899 by a surgeon named Walker. Bowditch, in his description of the condition, stated that he thought the lesion was operable, but he did not attempt surgical repair and his patient died one month afterward.

By summarizing the 26 cases I mentioned earlier, I hope to convince you that it is the very severely injured patient who is likely to have a traumatic rupture of the diaphragm. If a patient is seen because of the complications of a traumatic rupture of the diaphragm that occurred 10 years earlier, it is not likely that he will have forgotten the injury that produced the rupture. He may have spent a year in the hospital with fractures, as one of our patients did, and it is under these circumstances that evidence is obscured and difficult to interpret. It is in this very situation that we are loath, and I think wrongly so, to operate; the patient is very ill and has complicated problems involving fractures and other in-

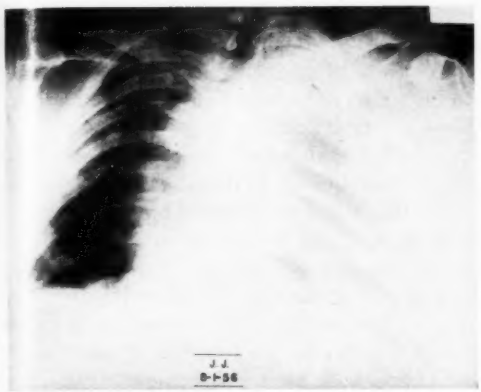


FIGURE 2. Case 2. Opacification of left hemithorax with deviation of mediastinum to the right. Tympanitic note to percussion on the left side suggested an intrathoracic hollow viscus, which was the stomach.

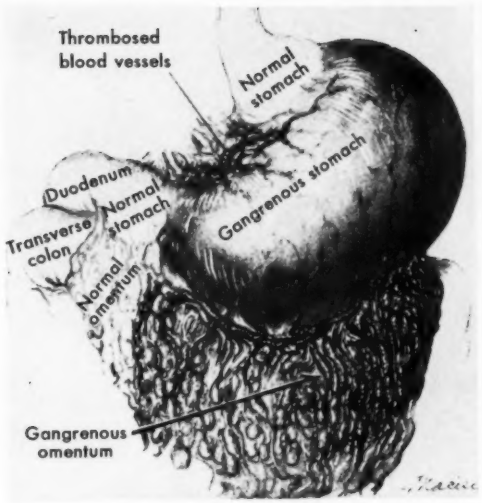


FIGURE 3. Drawing of the stomach following evisceration through a diaphragmatic rupture into the chest with subsequent gangrene, a situation very similar to that in case 2.

juries. I would like to convince you that these patients should be operated on, and that operation should be done as a relative emergency except in the most extenuating circumstances.

Illustrative Cases

Case 1—Figure 1a is a chest roentgenogram of a 23 year old man who was admitted to Ancker Hospital in 1957. He was dyspneal, with grunting, painful respirations. Pulse rate was 120, and blood pressure was 150/94. The abdomen was acutely tender and rigid, with rebound tenderness. The roentgenologist who saw the film called the abnormality an elevated diaphragm. The patient did not have fractures, which is very unusual in a situation like this, but he had been in an accident in which two persons were killed. Whenever a patient is seen who is severely injured and has an elevated diaphragm, one has to assume he has a traumatic rupture of the diaphragm; and this assumption will not be wrong very often.

The patient had a rupture of the spleen, and the gallbladder was also lacerated. An exploratory operation was performed through the abdomen, and a 10 cm. laceration of the diaphragm was found. The spleen and gallbladder were removed, and the diaphragm was repaired from below. The patient recovered uneventfully.

A roentgenogram made in the lateral decubitus position (figure 1b) can be very useful, and in this case it showed the fluid level above the diaphragm. Figure 1c is a film made 15 days after operation, at the time of the patient's dismissal from the hospital.

Repair of traumatic rupture of the diaphragm from the abdomen has been likened to shingling a roof from the attic, and I think this injury should not be repaired from below if it has been present for any length of time—say, more than a week. Adhesions will have formed which cannot be taken down from below. But when we strongly suspect the presence of an abdominal injury, we frequently do enter the abdomen. It would have been impossible in this case to perform cholecystectomy from the left side of the chest, and a thoracoabdominal incision would have been necessary. In a severely injured patient I think it is easier on the patient if one does not cut across the costal margin.

Case 2—Figure 2 is an x-ray of a 60 year old man who was admitted to University Hospitals 72 hours after a severe automobile accident. A tube had been placed in the thorax, and a diagnosis of hemothorax had been

FIGURE 4. Case 3. Admission chest film. Multiple loops of small bowel in lower right side of chest. Note old rib fractures on the right. A large portion of the right lobe of the liver in addition to small intestine was displaced through a rent in the right side of the diaphragm.

made. Little blood had drained, and the tube had been removed. Another tube was inserted when the patient was brought to the emergency room at University Hospitals, and some greenish material drained from it. The patient was comatose, and was thought to have a cranial injury. Breathing was very rapid. The left hemithorax was tympanitic on percussion, and the intern noted that he could hear the heart better on the right side than on the left. The patient was taken to the operating room, but he died en route. Autopsy revealed a rupture of the left diaphragm with gangrenous stomach in the chest and a thoracogastric fistula.

I think the point to remember in regard to this case is that it is worthwhile to pass a nasogastric tube if you suspect traumatic rupture of the diaphragm, for two reasons: (1) In this situation it will either not go into the stomach or, if you do get it in, it probably will prevent torsion. (2) If you are really lucky, the nasogastric tube will go right down and then up in the chest—in the stomach. Even when the stomach is in the chest, this will not always happen, but if it does the diagnosis is established.

Figure 3 is an artist's concept of what happens to the stomach in this situation. It rotates up so that the greater curvature becomes the highest part, and if it twists or if the hole in the diaphragm is relatively small the blood supply is cut off and gangrene results. Histologic examination of the stomach in the case depicted in figure 2 revealed gangrene through the entire wall. Strangulating obstruction occurred in one of the two patients described originally by Ambroise Paré, but not until eight months after injury. It can happen earlier. Strangulating obstruction is a common complication of traumatic rupture of the diaphragm, and in the case just described gangrene occurred within 72 hours following the accident.

Case 3—Figure 4 is the roentgenogram of a man who was admitted to University Hospitals with a history of tenderness in the right lower abdominal quadrant. Rigidity and rebound tenderness were elicited. He had vomited twice. The leukocyte count was 16,000. These findings did not tax the diagnostic acumen of the admitting intern, who suggested appendicitis—as I am sure many of us would. An exploratory operation was performed, and what the patient really had was traumatic rupture of the diaphragm. The rupture had occurred three years previously when the patient fell off a barn. He had been hospitalized for one year with a fractured right hip, a fracture of the right shoulder, and five fractured ribs on the right side. Repair of the diaphragmatic rupture was accomplished through a right thoracoabdominal incision. The reason for the pain in the right lower abdominal quadrant was tremendous tension on the mesentery of the small bowel. The patient recovered uneventfully.

Right-sided traumatic rupture of the diaphragm is very uncommon. There were only 10 cases reported in the American literature up to 1953, and in the present series there were three such cases.

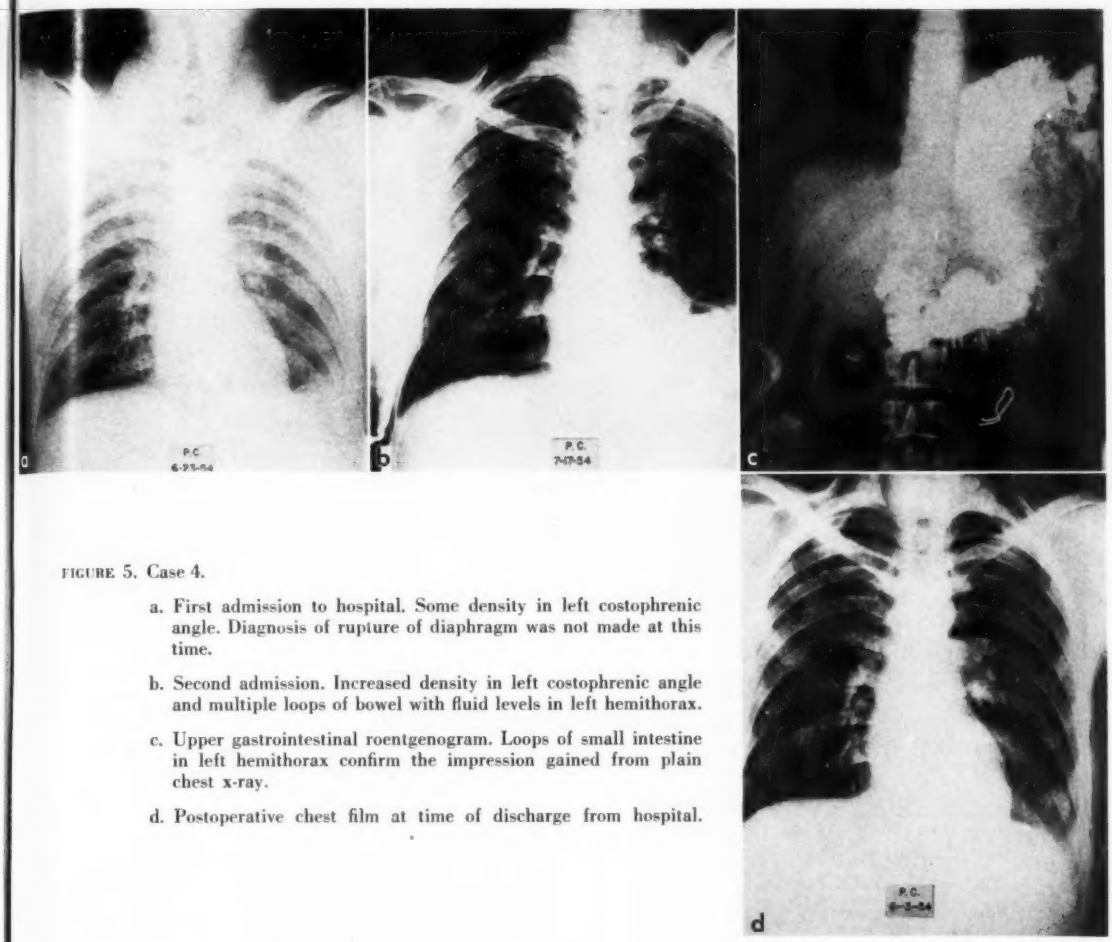


FIGURE 5. Case 4.

a. First admission to hospital. Some density in left costophrenic angle. Diagnosis of rupture of diaphragm was not made at this time.

b. Second admission. Increased density in left costophrenic angle and multiple loops of bowel with fluid levels in left hemithorax.

c. Upper gastrointestinal roentgenogram. Loops of small intestine in left hemithorax confirm the impression gained from plain chest x-ray.

d. Postoperative chest film at time of discharge from hospital.

Case 4—Figure 5a is the chest roentgenogram of a young man who was admitted to the hospital after a motorcycle accident. He had a fractured pelvis and a patellar fracture. After two weeks he was ready to be dismissed. The pelvic fracture was not too severe, and no one made anything of the blunting of the costophrenic angle. Three days after dismissal, the patient returned. He had been vomiting for 24 hours and had abdominal pain. An x-ray (figure 5b) showed fluid levels in the left hemithorax and an obvious increase in the fluid. Omentum can obliterate a rent in the diaphragm and then later this ruptures and there is difficulty. A nasogastric tube was inserted, and the patient responded quite well. An upper gastrointestinal roentgenogram (figure 5c) revealed small bowel displaced into the left hemithorax. Repair of the diaphragmatic rupture was accomplished through the thorax alone, and the patient was sent home, apparently well (figure 5d). Later the same year he returned again with nausea, vomiting, abdominal pain, rebound tenderness—acute abdomen. Exploration disclosed a gangrenous loop of bowel. A loop of bowel had gone through a rent in the mesentery and twisted, necessitating resection.

The lesson to be learned here is that if one is going to repair a diaphragmatic rupture

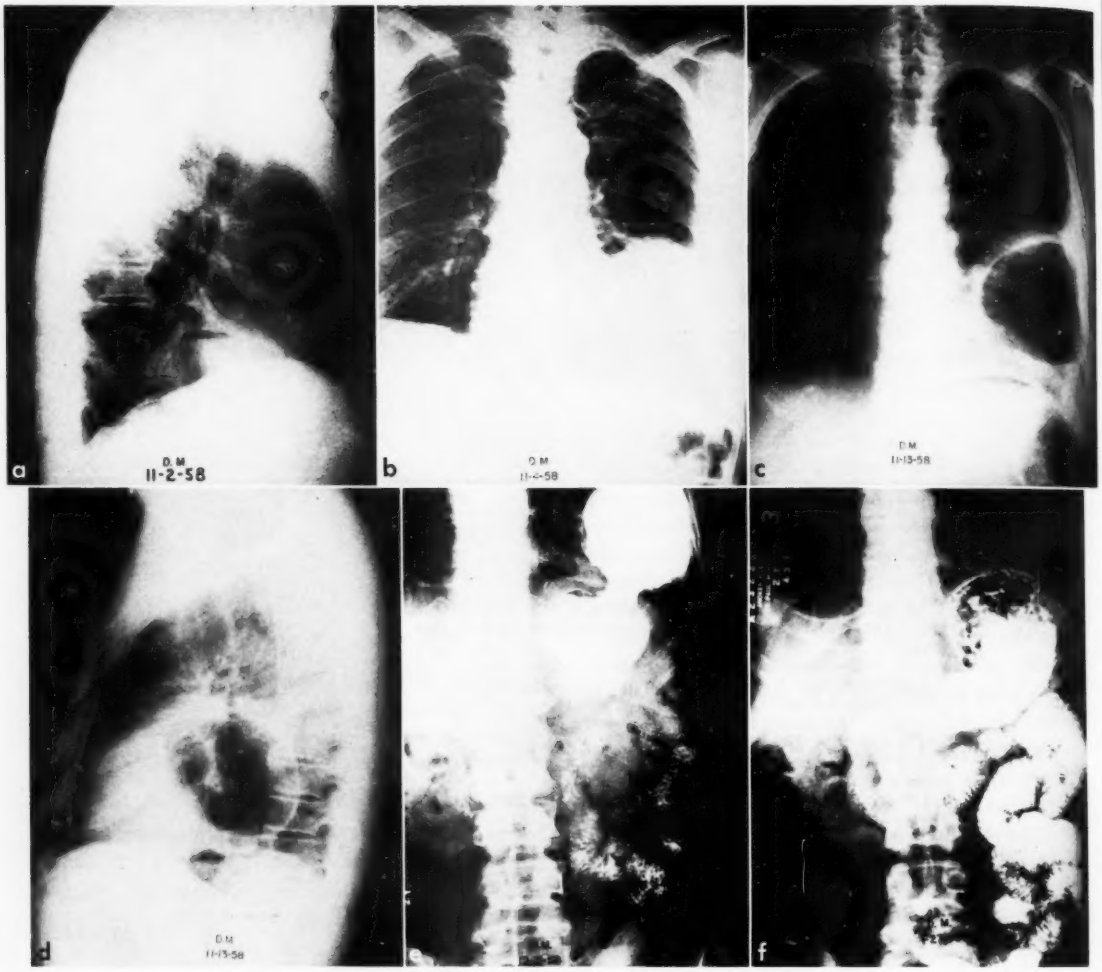


FIGURE 6. Case 5.

a. Lateral chest roentgenogram at time of admission to hospital. Density in lower lobe suggestive of pneumonia with a fluid level.

b. Two days later. Mass in left lower lung field suggestive of pneumonitis or atelectasis.

c. Nine days later. Large air-filled cavity in left lower hemithorax was interpreted as lung cyst.

d. Lateral roentgenogram revealing air-filled cystic structure.

e. Upper gastrointestinal roentgenogram reveals the true nature of the air-filled "cyst" to be stomach eviscerated through a rather small rent in the diaphragm.

f. Postoperative upper gastrointestinal x-ray. Normal location of stomach after excision of eviscerated portion of stomach and repair of diaphragm.

from the thorax one still must make sure additional injury is not present in the abdominal cavity. This patient had a fractured pelvis, and probably a spicula of bone divided the small bowel mesentery; a loop of bowel slipped through it at a later time and caused the gan-

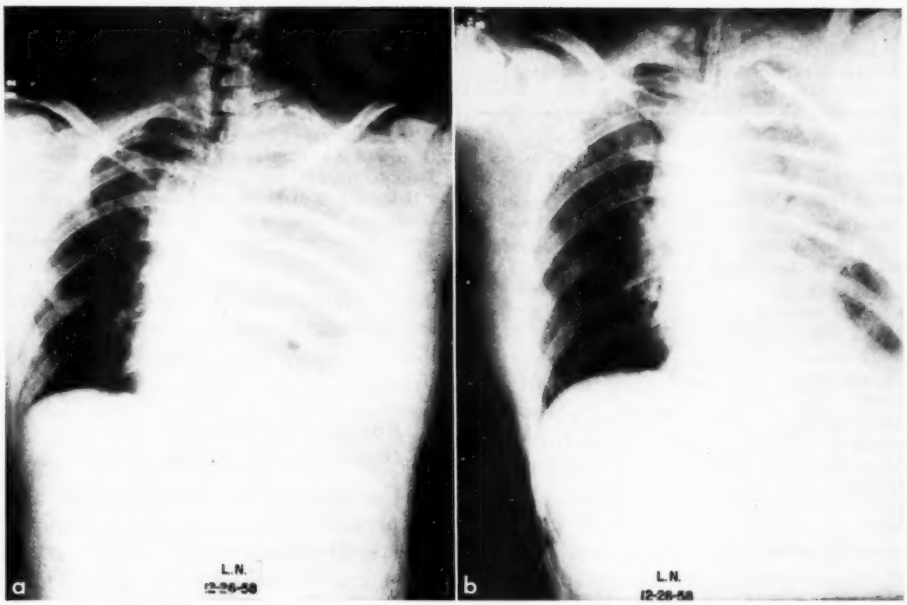


FIGURE 7. Case 6.

a. Chest film made immediately following admission to the hospital. Slight elevation of left diaphragm and opacification of left hemithorax with mediastinal shift to the right.

b. Film made immediately following insertion of a thoracostomy tube, and aspiration of 2000 cc. of blood in a very short period. An air-filled viscus in the left hemithorax is now obvious. At operation this proved to be the stomach. The spleen was also displaced into the left hemithorax and was ruptured, accounting for the extensive hemorrhage.

grenous obstruction. It is easier to repair a ruptured diaphragm through the chest, but one must make sure that additional pathology does not reside within the abdomen.

Case 5—The x-ray in figure 6a is of a man who was admitted to the medical service at Ancker Hospital with fever, elevated leukocyte count, and pain in the chest on breathing. You know that I am going to get around to traumatic rupture of the diaphragm eventually, but at the time this film was made the diagnosis was pneumonia. You can see a fluid level that was overlooked until we reviewed the x-ray later. A few days later (figure 6b) a consolidation or collapsed lower lobe was seen. Thoracentesis yielded bloody fluid. The patient was responding fairly well to medical therapy and seemed to be recovering. Films made nine days later (figure 6c and d) showed a huge cavity seemingly unrelated to the diaphragm. Close questioning of the patient elicited a history of a stab wound in the chest for which he had been hospitalized at Cook County Hospital in Chicago. He said he had signed out of the hospital the day after he was admitted and had not been bothered by the wound. He signed out of Ancker Hospital, too, against advice, but he returned two weeks later complaining of passing blood per rectum. The hemoglobin level was 7 gm.; it had been normal when he left the hospital. An upper gastrointestinal series (figure 6e) was made, and revealed that the air-filled "cyst" was stomach eviscerated through a small rent in the diaphragm. Repair of the diaphragmatic rupture with resection of the displaced stomach was accomplished through the chest. The patient has remained well. A postoperative upper gastrointestinal roentgenogram is reproduced in figure 6f.

TABLE 1

TRAUMATIC RUPTURE OF THE DIAPHRAGM, ANCKER HOSPITAL AND UNIVERSITY HOSPITALS, 1940 to 1958

Total cases	26
Males	22
Females	4
Children (under 16 years)	4
Mode of injury	
Indirect blunt trauma	21
Direct penetrating wound	5
Mechanism of injury	
Automobile accident	20
Fall from height	1
Gunshot wound	2
Knife wound	2
Unknown	1
Associated injuries	
Fractures	
Pelvis	12
Extremity	11
Rib	10
Spine	1
Visceral lacerations	
Spleen	9
Liver	4
Kidney	2
Stomach	2
Pancreas	1
Colon	1
Mesentery	1
Thoracic visceral injuries	
Contusion of lung	3
Severe cerebral injuries	7
Organs eviscerated	
Stomach	1
Stomach and omentum	7
Stomach, omentum and colon	1
Stomach, omentum, colon and spleen	3
Stomach, omentum, colon and intestine	3
Stomach, omentum, colon and liver	1
Stomach, omentum and spleen	3
Colon	1
Colon and intestine	1
Liver, gallbladder and intestine	1
None	4

Case 6—Figure 7 illustrates an interesting case. The patient was admitted to Ancker Hospital in extremis. Blood pressure could not be recorded. Transfusion of blood was started, and a nasogastric tube was inserted. An intercostal catheter was inserted on the left side, and 2000 cc. of blood poured out. At emergency operation the patient's stomach was found to be in the chest, together with the spleen. The spleen was ruptured. As soon as the splenic pedicle was clamped, the patient's blood pressure returned to normal. She made an uneventful recovery but was hospitalized for a lengthy period because of associated fractures.

TABLE 2

MISTAKEN DIAGNOSES IN RUPTURE OF THE DIAPHRAGM

Left lower lobe pneumonia
Atelectasis of lower lobe
Pneumothorax
Eventration of diaphragm
"Obliteration of costophrenic angle"
"Deformity of diaphragmatic contour"
Lung cyst

Review of 26 Cases of Diaphragmatic Rupture

The 26 cases of traumatic rupture of the diaphragm seen at University Hospitals and Ancker Hospital over an 18 year period are summarized in tables 1 through 4. Two of the women were pregnant at the time of injury (one four months and one six months). These two women, both of whom had other injuries (one a fractured pelvis), delivered normal infants from below at term.

The injury was indirect blunt trauma in 21 cases and a direct penetrating wound in five (table 1). The automobile was implicated in most cases. Other patients were injured in a fall or by a gunshot or knife wound. In one case, that of a man admitted in extremis, we were unable to establish the mode of injury.

Fractured pelvis was the most common injury associated with diaphragmatic rupture. Twelve of the 21 patients with injuries due to blunt trauma had fracture of the pelvis. Eleven of these 12 patients also had fractures of one extremity or more. Fractured ribs were quite common, and spinal fracture very rare.

When we see a patient who has been in an automobile accident and is severely injured and has a fractured pelvis, one of the first things we think of is traumatic rupture of the diaphragm. We think it is important to make that diagnosis promptly and institute proper treatment.

Laceration of the spleen occurred in nine cases, and laceration of the liver in four. The

TABLE 3

MORBIDITY AND MORTALITY IN 12 CASES IN WHICH TREATMENT WAS DELAYED MORE THAN 48 HOURS

Symptomatic in interim	11
Intermittent partial intestinal obstruction	5
Simple complete intestinal obstruction	4
Strangulating obstruction	1
Strangulation of omentum	1
Thoracogastric fistula	1
Gastric hemorrhage	1
Pneumonia and atelectasis	1
Acute respiratory embarrassment	1
Mortality rate	25% (3 deaths)

TABLE 4

TOTAL MORTALITY AND CAUSES OF DEATH IN 26 CASES OF RUPTURE OF THE DIAPHRAGM

Total mortality	31% (8 cases)
Before operation	7
After operation	1
Causes of death	
Multiple injuries and shock	4
Strangulation and gangrene of stomach	1
Complete obstruction of small bowel	1
Pneumonia and atelectasis	1
Postoperative aspiration	1

kidney and even the pancreas can be lacerated in the injuries that cause traumatic diaphragmatic rupture. Seven patients had severe cerebral injuries, and two of the patients were unconscious when they were taken to the operating room for repair of the diaphragmatic rupture.

The stomach, colon and small bowel are the three viscera that most commonly are found in the chest in traumatic diaphragmatic rupture, but any combination is possible. The stomach was in the chest in 19 cases, the colon in 10, and the small bowel in five.

Mistakes in diagnoses, based on roentgenograms, are listed in table 2. When you have a patient who is severely injured and these diagnoses are considered, it might be worthwhile to think also of traumatic rupture of the diaphragm, even though the diaphragm looks perfectly normal.

In approximately half the cases, treatment was delayed more than 48 hours (table 3). Eleven of these 12 patients were symptomatic in the interim. Intermittent partial intestinal obstruction was documented in five cases, and simple complete intestinal obstruction (unrelenting) in four. Other morbidity included strangulating obstruction, strangulation of omentum, thoracogastric fistula, gastric hemorrhage, pneumonia and atelectasis, and acute respiratory embarrassment, each of which occurred in one case. The mortality rate for the group in which treatment was delayed more than 48 hours was 25 per cent.

The over-all mortality rate was 31 per cent (table 4). Seven patients died before reaching the operating room. Admittedly these were severely ill patients with multiple injuries (four of them were in shock), but I think today some of these patients could be saved. Two of them died at a time when blood was not used as much as it is now—in the early 1940s. One patient who died with strangulation and gangrene should have recovered. Another had a small bowel obstruction that was completely overlooked; not even a chest x-ray was made. Pneumonia and atelectasis accounted for one death as a result of collapse of the lung. There is one tragic case here of a patient who died after operation, in 1943, from aspiration on the operating table after the reparative procedure; this was before cuffed intratracheal tubes were used, before nasogastric suction was used routinely, and I am certain that this sort of thing would not happen today.

Summary and Conclusions

Twenty-six cases of traumatic rupture of the diaphragm are reported which were seen at the University of Minnesota Hospitals, Minneapolis, and the Ancker Hospital, St. Paul, from 1940 through 1958. Three-fourths of the patients were seen after 1952.

Blunt trauma, most frequently associated with pelvic fracture, accounted for rupture of the diaphragm in 21 of the 26 cases. The left diaphragm was ruptured in 23 instances, the right diaphragm twice, and both sides of the diaphragm once.

Diagnosis of diaphragmatic rupture depends on a history of severe injury, usually in an automobile accident. The five physical

signs first outlined by Bowditch in 1853 are extremely useful. The use of serial roentgenograms of the chest, gastrointestinal series, barium enema and roentgenograms of the chest after insertion of an opaque nasogastric tube, alone or in combination, usually establishes the diagnosis.

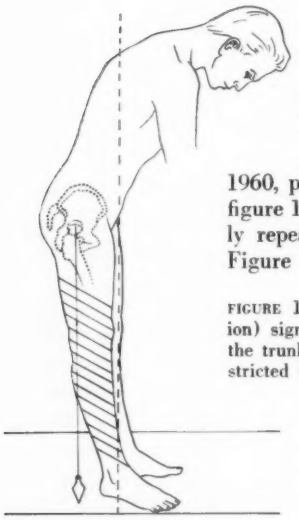
Delay in repairing diaphragmatic rupture markedly increases morbidity and mortality. Of the 19 patients who came to operation, one died, from postoperative aspiration. The over-all mortality rate was 31 per cent (eight deaths). Seven patients died without surgical exploration. It is felt that five of these seven patients could be salvaged at present with prompt surgical intervention.

The experience reported herein would indicate that it is quite rare for a patient to be asymptomatic after traumatic rupture of the diaphragm if this abnormality is not repaired, even though he may be well enough to leave the hospital. The late complications in patients with unrepaired rupture of the diaphragm frequently are severe and life-endangering and appear almost inevitable.

To repair the diaphragm, the abdominal approach, the thoracic approach and the thoracoabdominal approach have all been used. The thoracic approach affords the best exposure for diaphragmatic repair but may be deficient unless great care is taken in exposing intraabdominal injuries. The phrenic nerve was neither crushed nor divided in any instance. Closure was accomplished without pericardiac or other forms of grafting, and there have been no late recurrences.

Part 3 of this group of papers on Emergency Surgery for General Physicians will appear in the June issue.

Correction



In the article "Determinations of sciatic nerve tension" by Arthur A. Michele, M.D. (November 1960, pages 488 to 502), figure 18 was inadvertently repeated as figure 15. Figure 15 is shown here.

FIGURE 15. Withdrawal (flexion) sign positive. Flexion of the trunk on the pelvis is restricted to about 45 degrees.

SCIENTIFIC EXHIBIT

Radioautography in Gastric Cancer

N. B. ACKERMAN, A. S. McFEE, B. T. SANTORO AND O. H. WANGENSTEEN

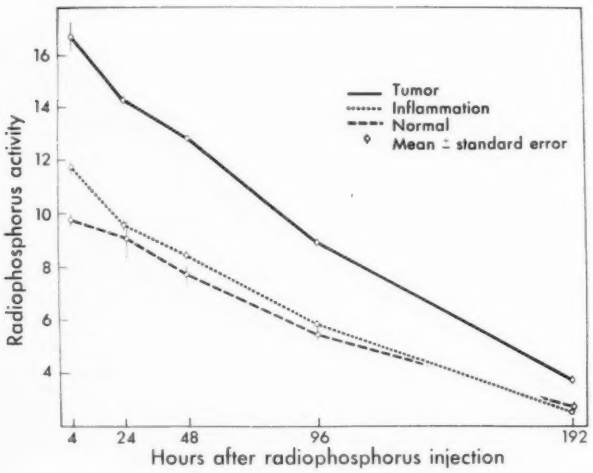
Department of Surgery, University of Minnesota Hospitals, Minneapolis

Adapted from an exhibit presented at the Clinical Congress, American College of Surgeons, San Francisco, California.

Supported by the American Cancer Society and the Atomic Energy Commission.

Rationale

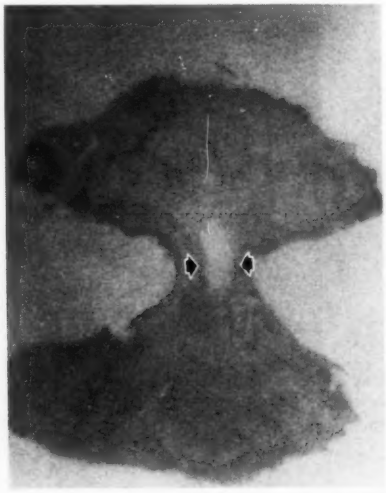
ALTHOUGH all tissue contains phosphorus, malignant tissue has an increased phosphorus uptake. Surface counting with a Geiger-Müller counter shows that radiophosphorus (P^{32}) concentrates up to five times more heavily in cancerous tissue than it does in other tissue.



Surface radiophosphorus activities of tumorous, inflammatory and normal areas.

In vitro radioautographs of excised gastric tissue indicate the presence of cancer by areas of increased darkening due to more intense radiophosphorus accumulation. The technic of in vivo balloon radioautography has been developed to adapt this principle to a diagnostic test for gastric cancer.

In vitro radioautograph of stomach with large gastric cancer.

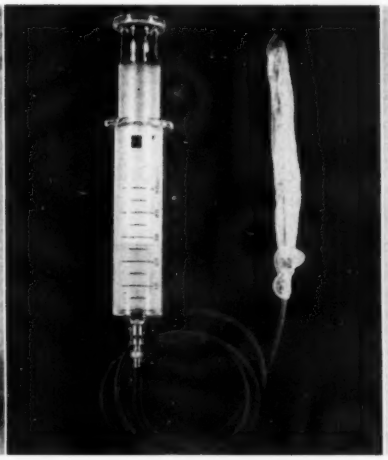


In vitro radioautograph of stomach with benign gastric ulcer.

Method

From 12 to 24 hours before the test, 500 μc of radiophosphorus is administered intravenously to the patient. A thin, expandable latex balloon coated on the inside with a photosensitive emulsion is attached to a nasogastric tube. Intubation is performed in a darkroom. The balloon is inflated with from 600 to 900 cc. of air.

Injection.



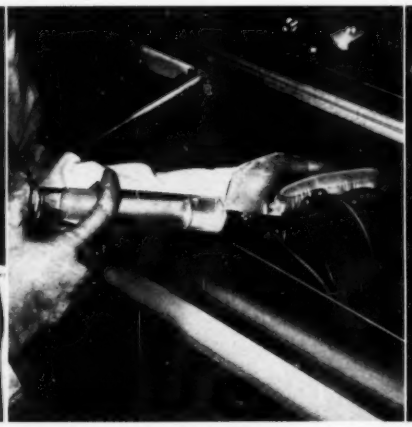
Apparatus.

Intubation.

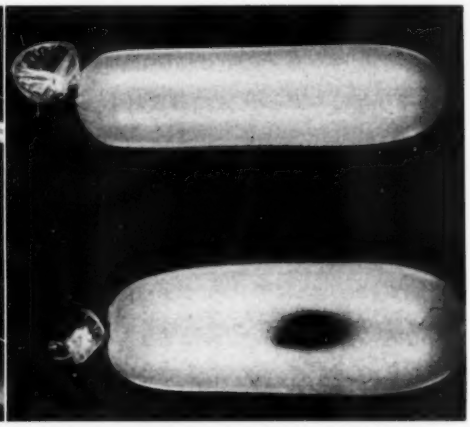
The balloon in the patient's stomach is exposed during a four hour period. Sedation and anticholinergics are used. Processing is performed in a standard manner. Developing solutions are inserted via the nasogastric tube.

Evaluation of test: A darkened spot on the balloon implies contact with malignant tissue. The balloon retains its white color where cancer is absent.

Exposure.



Processing.



Evaluation.

Results

The following chart shows the results of in vivo gastric radioautography for gastric cancer in 232 patients whose clinical or x-ray diagnosis or both indicated normal or pathologic conditions of the stomach.

Final Clinical Diagnosis	Number of Patients	Gastric X-ray Diagnosis	Number of Patients	Gastric Balloon Diagnosis	Number of Patients
Gastric cancer	16	Cancer Possible cancer Benign ulcer	12 3 1	Cancer Benign	14 2
Benign ulcer	41	Benign ulcer Cancer Possible cancer Normal stomach	35 2 3 1	Benign Cancer	36 5
Achlorhydria	101	Normal stomach	101	Benign	101
Pernicious anemia	34	Normal stomach	34	Benign	34
Gastric polyps	9	Gastric polyps	9	Benign	9
Hypertrophic rugae	8	Hypertrophic rugae	8	Benign	8
Gastritis	5	Gastritis Normal stomach	3 2	Benign Cancer	4 1
Postoperative gastric deformity	3	Postoperative gastric deformity	3	Benign	3
Leiomyoma	1	Leiomyoma	1	Benign	1
Normal stomach	14	Normal stomach Cancer	12 2	Benign	14
TOTAL	232		232		232

Results

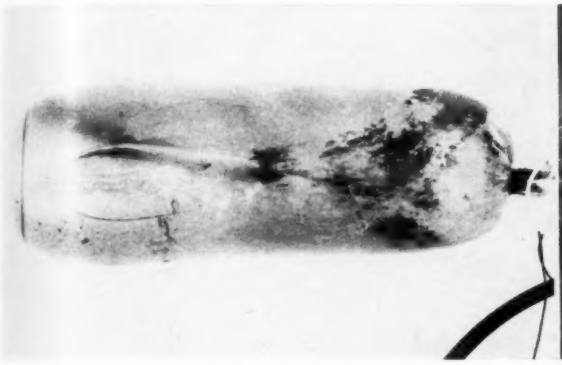
History: Fifty year old white woman; hematemesis with no prior symptoms.

Laboratory data: Thirty-four degrees free acid with histaminic stimulation.

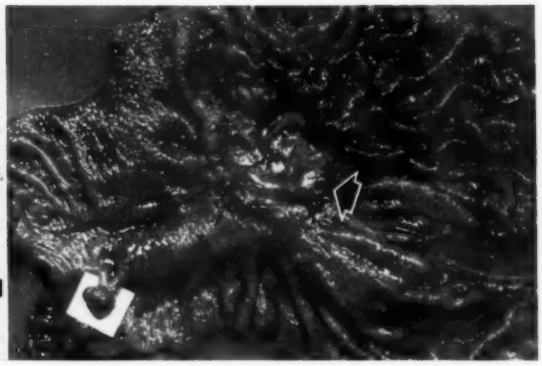
X-ray findings: Benign gastric ulcer and antral polyp.

Balloon evaluation: Positive for cancer.

Pathologic report: Ulcerating cancer with spread to only one lymph node. Benign polyp.



Balloon evaluation.



Specimen.

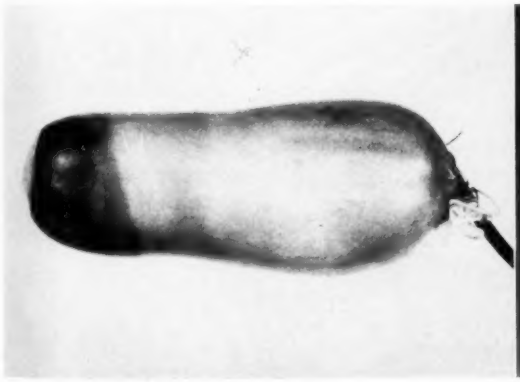
History: Fifty-one year old white man; nausea and vomiting for four weeks; gastroenterostomy 25 years ago.

Laboratory data: Fifty-four degrees free acid with histaminic stimulation.

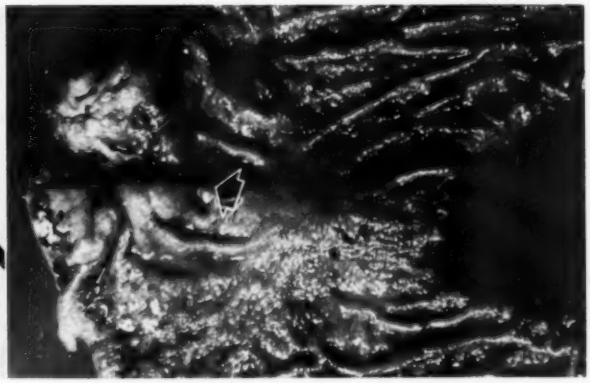
X-ray findings: Stomal ulcer. Lesion in antrum (cancer?).

Balloon evaluation: Positive for cancer.

Pathologic report: Adenocarcinoma in antrum with spread to lymph nodes and omentum.



Balloon evaluation.



Specimen.

Results

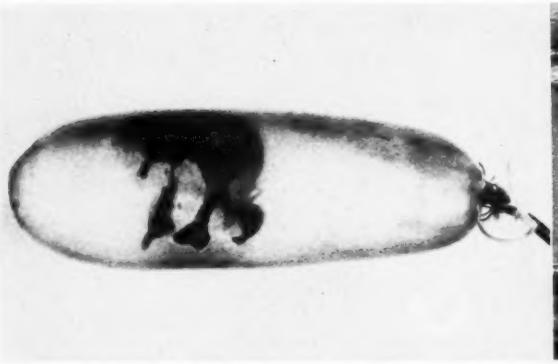
History: Sixty-seven year old white woman; two month history of epigastric pain and tarry stools.

Laboratory data: Achlorhydria.

X-ray finding: Extensive cancer in fundus.

Balloon evaluation: Positive for cancer.

Pathologic report: Adenocarcinoma with spread to regional lymph nodes.



Balloon evaluation.

Specimen.

History: Seventy-eight year old white man; long history of epigastric pain; 16 lb. weight loss in a year.

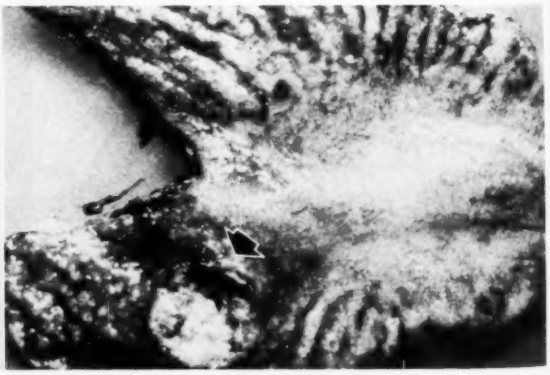
Laboratory data: Achlorhydria for 28 years.

X-ray findings: Yearly gastrointestinal series negative for cancer for 15 years; recent films showed cancer in greater curvature of stomach.

Balloon evaluation: Positive for cancer.

Pathologic report: Adenocarcinoma without spread.

Balloon evaluation.



Specimen.

Recent Experiences in Diagnosing and Treating Pernicious Anemia

WALTER G. UNGLAUB,* AMOS L. PREVATT† AND GRACE A. GOLDSMITH‡

Tulane University School of Medicine, New Orleans

UNTIL recently, the diagnosis of pernicious anemia has been made primarily on a clinical basis with the assistance of a few pertinent but not entirely specific laboratory findings. The criteria for diagnosis included: (1) a macrocytic anemia, with poikilocytosis, anisocytosis and polychromatophilia of the red cells, leukopenia, with multilobular nuclei in the granulocytes, and thrombocytopenia; (2) megaloblastic maturation arrest of the bone marrow; and (3) the absence of free hydrochloric acid in the gastric juice after stimulation with histamine. The demonstration of neurologic findings compatible with lesions of the posterior and lateral columns of the spinal cord, i.e., subacute combined degeneration, made the diagnosis more certain, but such changes were not always present; nor was glossitis or the classic lemon-yellow discoloration of the skin always observed. In relatively few instances was it feasible to demonstrate the absence of intrinsic factor in the gastric secretion. This required administering the patient's gastric juice in combination with a source of extrinsic factor (vitamin B_{12} when it became available) to a patient with pernicious anemia in relapse and observing whether hematologic response occurred.

The development of the Schilling test[1] for studying the absorption of vitamin B_{12} from the intestinal tract has contributed significantly to accuracy of diagnosis. With increasing use of this technic, a number of cases diagnosed as pernicious anemia and reported in the literature as such have been found to be not this disease at all but, rather, other types of megaloblastic anemia. Some of these anemias, like pernicious anemia, are due to malabsorption of vitamin B_{12}, but the malabsorption is not the result of absence of intrinsic factor from the gastric secretion. We[2] pointed out in one study that one-third of a group of 21 patients with megaloblastic anemia due to primary intestinal malabsorption

*Associate Professor of Medicine; †Instructor in Medicine; ‡Professor of Medicine, Tulane University School of Medicine, New Orleans, Louisiana. Dr. Prevatt's present address is Pensacola, Florida.

This study was supported in part by grants from the Nutrition Foundation, the Williams Waterman Fund of the Research Corporation, and the Division of Research Grants and Fellowships, United States Public Health Service (grant A-1).

WALTER G. UNGLAUB

GRACE A. GOLDSMITH

of vitamin B_{12} were considered to have typical pernicious anemia prior to the Schilling test.

The purpose of this paper is to present and discuss our observations in a group of 45 patients in whom the results of the Schilling test were compatible with the diagnosis of pernicious anemia. The group included three subjects in whom macrocytic anemia developed as a result of total or subtotal gastrectomy. The role of intrinsic factor in vitamin B_{12} metabolism also will be discussed.

Materials and Methods

The 45 patients on whom this report is based were seen in the Nutrition Clinic of Tulane University and in the Charity Hospital of Louisiana, New Orleans. Many of the patients had been under treatment in the Nutrition Clinic for years before the Schilling test was introduced.

The Schilling test was performed during the years from 1956 to 1958, inclusive. All tests were carried out in a metabolism ward to insure accuracy in the collection of specimens. The technic of the procedure was that originally described by Schilling. Two micrograms of vitamin B_{12}-Co^{60} containing 0.5 μc of radioactivity was given orally in solution. Two hours later a "flushing dose" of 1000 μg. of nonradioactive vitamin B_{12} was given intramuscularly. Urine was collected for 24 hours following administration of the labeled vitamin, and the radioactivity was measured. Three or four days following the initial test, the procedure was repeated with the addition of 20 mg. of an active intrinsic factor concentrate to the solution of vitamin B_{12}-Co^{60}.

Concentration of vitamin B_{12} in the serum of patients in relapse was measured by the microbiologic method of Rosenthal and Sarett,[3] although not necessarily at the same time that the Schilling test was performed. In some instances, the serum vitamin B_{12} activity was determined several years prior to performance of the Schilling test.

Distribution of Patients as to Sex, Race and Age

Distribution of the 42 patients who were found to have pernicious anemia was determined with respect to sex, race and age at onset of the disease. Findings are shown in table 1. The duration of the disease prior to performance of the Schilling test is also indicated. Twenty-six of the patients with pernicious anemia were white; 16 were Negro. Of the patients who had macrocytic anemia following gastrectomy, two were white men; the third was a white woman.

Other observers have stated that pernicious anemia is uncommon in the Negro race. Kampmeier and Cameron[4] reported the ratio of white-to-Negro patients with pernicious anemia in this same hospital as 7:1, while the ratio at Cook County Hospital, Chicago, was reported to be 5:1.[5] This series, as well as our experience with other patients not included in this report, does not support such a marked preponderance of the disease in the white race.

In the group of patients we studied, there was no apparent sex difference in the incidence of pernicious anemia. It does seem that the disease became manifest at an earlier age in the Negro than in the white race. The difference in age at onset between the two groups is statistically significant: $P \backsim 0.001$ by the "pooled median" test. It has been stated that pernicious anemia rarely appears before the age of 30.[6] Only three patients of this series were 30 years old or less at the time of onset of their disease. The youngest of these, a Negro man, was 22 years old when the diagnosis of pernicious anemia was made. The other two young patients were white women; one was 23 and the other was 30 years old at the time the disease developed.

TABLE 1

AGE, RACE AND SEX DISTRIBUTION OF PATIENTS WITH PERNICIOUS ANEMIA

GROUP	PATIENTS (NUMBER)	AGE AT ONSET OF DISEASE		DURATION OF DISEASE PRIOR TO THE SCHILLING TEST	
		Range (Years)	*Average (Years)*	*Range (Years)*	*Average (Years)*
Men					
White	14	42-72	60.2	2-14	6.7
Negro	7	22-60	46.7	1-16	5.6
Women					
White	12	23-73	54.1	0-26	7.3
Negro	9	32-74	48.8	0-6	1.8

Little information concerning the ethnic background of the white patients in this group could be obtained. Most of them were natives of southern Louisiana and of Anglo-Saxon and mixed European ancestry.

Clinical Manifestations of Pernicious Anemia

The duration of symptoms prior to initial treatment ranged from two months to more than two years. In some instances, the onset of symptoms was rapid; in others, it was very insidious. There was no apparent relationship between rapidity of onset and response to treatment or the development of neurologic complications.

Weakness was a predominant complaint of all patients in this series. In some instances, it was of only moderate degree; in others, the patient was completely bedridden. There was usually a prompt and sometimes amazing improvement when therapy was begun, preceding by several days any demonstrable change in the blood picture.

Gastrointestinal symptoms were among the most common complaints. Anorexia, nausea, vomiting, vague indigestion and midepigastric pain were noted singly or in various combinations by every patient. In 20 subjects, there was a history of weight loss. Diarrhea occurred in four instances. Glossitis, characterized by redness of the tongue and atrophy of the filiform papillae, was encountered in 28 patients.

Symptoms second in frequency to those referable to the gastrointestinal system were of cardiovascular origin. Dyspnea was the most common finding. Slight edema of the feet and ankles also was frequently observed, while frank congestive heart failure was present in one patient. Angina pectoris was the presenting complaint in five patients. When cardiovascular symptoms were prominent, confusion in diagnosis not infrequently resulted. The following case is cited as an example.

A 64 year old white man was first seen in a general medicine clinic with complaints of dyspnea on exertion, orthopnea, pedal edema, and chest pain typical of angina pectoris. He was found to have mild diabetes, arteriosclerosis and a parkinsonian tremor. A complete blood count showed the presence of definite macrocytic-normochromic anemia of moderately severe degree. These findings were recorded in the patient's chart but apparently were overlooked by the attending physician, who arrived at a diagnosis of arteriosclerotic heart disease with coronary artery insufficiency. Digitalis, vasodilating drugs and a diabetic diet were prescribed. The diabetes was easily controlled but the cardiovascular complaints persisted during the ensuing months, increasing in severity. After one year of unsuccessful therapy, another observer noted that anemia had been present at the time of the first visit. Further investigation revealed that the anemia had become much more severe. Hemoglobin was 6.3 gm. per 100 ml., and the mean corpuscular volume (MCV) was 116 μ^3. The concentration of vitamin B_{12} in the serum was 30 $\mu\mu$g. per milliliter. The bone marrow was not typically megaloblastic. Oral

administration of 3000 μg. of crystalline vitamin B_{12}, as part of a special study, was followed by a marked reticulocyte response and an increase in erythrocytes. Oral administration of 1000 μg. vitamin B_{12} once weekly was instituted and has been continued for almost eight years, with complete remission of the anemia and disappearance of all cardiovascular symptoms. Serum vitamin B_{12} levels have been maintained within the normal range. A Schilling test performed five years after the initiation of therapy showed 3.3 per cent excretion after administration of vitamin B_{12}-Co^{60} alone and 9.6 per cent excretion when intrinsic factor concentrate was added.

Fever is often found in patients who have untreated pernicious anemia. It is usually of a low-grade, sustained type, seldom exceeding 100° F. However, in three patients in this series, fever was of a septic type, often reaching high levels. When this occurred, confusion in diagnosis resulted. In one patient, fever was as high as 103.6° F. and of the daily relapsing type. Extensive studies failed to uncover any infection as the cause for the elevation of temperature. A clinical diagnosis of pernicious anemia was proposed, and the patient was given 3000 μg. of crystalline vitamin B_{12} orally. Within four days the patient's temperature was normal, and there was marked subjective and objective improvement. This was followed by an excellent reticulocyte and erythrocyte response. The patient has now been maintained in clinical remission for more than eight years.

Damage to the central nervous system is the most serious complication of pernicious anemia. Evidence of subacute combined degeneration of the spinal cord was found in 12 patients of this series, while peripheral neuritis was present in seven. One patient had diminished vibratory sensation in both lower legs without other evidence of neurologic disease. Twenty-four members of the group complained of paresthesias of the hands or feet or both, but there was no objective evidence of nervous system involvement.

Of the 12 patients with subacute combined degeneration of the spinal cord, only six were found to have a typically megaloblastic bone marrow at the time of admission to the hospital. One patient had no significant anemia; the hemoglobin concentration was 14.0 gm. per 100 ml. but the erythrocytes were definitely macrocytic (MCV, 135 μ^3). He gave a history of having taken a proprietary multivitamin preparation which contained folic acid but no effective form of vitamin B_{12}.

Three patients had permanent neurologic disability due to the delay in arriving at a proper diagnosis. In one of these, the disease had been diagnosed as multiple sclerosis without adequate evaluation of the hematologic status. This patient had been given folic acid by the attending physician. By the time the correct diagnosis was established and proper therapy instituted, neurologic disease had progressed to the point of severe and permanent disability. In the second patient, only slight normocytic anemia was present (hemoglobin, 10.8 gm. per 100 ml.; MCV, 88 μ^3), and the bone marrow was found to be normoblastic. The patient emphatically denied any type of previous therapy. A diagnosis of hysteria was made, to be changed only by the results of the Schilling test. In the third patient, diagnosis was delayed by the failure to demonstrate macrocytosis of erythrocytes in the peripheral blood and megaloblastic change in the bone marrow.

Laboratory Findings in Pernicious Anemia

All patients in this series were found to have gastric achlorhydria, which did not respond to stimulation by histamine. In the majority of instances, true achylia gastrica appeared to be present, as very little or no gastric secretion could be obtained when aspiration was performed.

Findings in the peripheral blood were highly variable, since many subjects had received treatment prior to being referred to us and many were in complete remission. In some patients who had received no previous therapy as far as could be determined, only slight degrees of anemia were present. In two such patients, the anemia was normocytic-normochromic in type, and in one of these the bone marrow was not typically megaloblastic. In

TABLE 2

EXCRETION OF VITAMIN B_{12}-Co^{60} (THE SCHILLING TEST)

GROUP	PATIENTS (NUMBER)	EXCRETION AFTER ADMINISTRATION OF VITAMIN B_{12}-Co^{60} ALONE		EXCRETION AFTER ADMINISTRATION OF VITAMIN B_{12}-Co^{60} PLUS INTRINSIC FACTOR	
		Range (Per cent)	*Average (Per cent)*	*Range (Per cent)*	*Average (Per cent)*
Men					
White	14	0.1-3.3	0.7	7.7-21.3	14.0
Negro	7	0.2-2.8	0.8	9.9-18.6	13.1
Women					
White	12	0.2-1.3	0.7	6.2-18.2	11.6
Negro	9	0.2-1.4	0.8	5.8-23.8	12.9
All patients	42	0.1-3.3	0.9	5.8-23.8	12.9

three patients, it was felt that the peripheral blood and bone-marrow findings had been altered by previous administration of folic acid.

Megaloblastic changes in the bone marrow were demonstrated on at least one occasion during relapse in 31 of the 45 patients. Bone marrow was not examined in seven patients; in seven other patients the marrow was reported to be normoblastic or not diagnostic. Five of these subjects were seen initially after remission of their anemia had been induced by therapy.

Although most of the patients were noted to have a sallow or yellowish tinge to the skin, serum bilirubin determinations were recorded during relapse in only seven instances. In each of these, concentrations of bilirubin, predominantly of the indirect type, were increased, ranging from 1.3 to 5.8 mg. per cent.

The concentration of vitamin B_{12} in serum during relapse was measured in 20 patients. Values ranged from 0 to 80 $\mu\mu$g. per milliliter, with an average of 40 $\mu\mu$g. The normal range of values for this procedure in our laboratory is from 80 to 720 $\mu\mu$g. per milliliter, with an average of 450 $\mu\mu$g. Values below the normal range may be encountered in conditions other than pernicious anemia in relapse, such as primary intestinal malabsorption of vitamin B_{12} or the rare case of deficient dietary intake of this vitamin of many years' duration.

Results of the Schilling Test

The results of the Schilling test, which confirmed the diagnosis of pernicious anemia in the patients included in this study, are given in table 2. These values are comparable to those reported by other investigators in patients with pernicious anemia. Excretion of vitamin B_{12}, when given alone, is usually less than 1 μg. in 24 hours and rarely above 2 μg., while excretion is greater than 6 μg. when intrinsic factor is given in conjunction with vitamin B_{12}. In only one instance did the administration of intrinsic factor fail to raise the excretion of vitamin B_{12}-Co^{60} above 6 per cent. However, since excretion in the first part was only 0.2 per cent, excretion of 5.8 per cent of the dose following administration of vitamin B_{12} with intrinsic factor concentrate was considered to be evidence of a definite increase in absorption compatible with the diagnosis of pernicious anemia.

Medical Conditions Complicating Pernicious Anemia

Among medical conditions found in association with pernicious anemia in these subjects were diabetes mellitus in two patients, hiatus hernia in two, and postoperative myxedema in one. One patient who was found initially to have a moderately severe macrocytic anemia and a megaloblastic bone marrow responded promptly to vitamin B_{12} ther-

apy and attained a hemoglobin concentration of 18.6 gm. per hundred milliliters. Additional studies then established the diagnosis of primary polycythemia. This necessitated the addition of radiophosphorus and phlebotomy to the patient's therapeutic regimen. Acute gouty arthritis developed in the right toe of another subject who had an excellent hematopoietic response to vitamin B_{12} therapy. This patient, who was 72 years old, had experienced no previous acute attack of gout. Levels of uric acid in the serum reached 8.7 mg. per cent during the acute episode but gradually declined to normal and have remained within the normal range for the past five years. High levels of uric acid in serum during periods of relapse in pernicious anemia, with further elevation in response to therapy, have been noted previously,[7] as has the occurrence of typical gouty arthritis during the initial period of treatment.[8]

One Negro woman, admitted with severe anemia and a megaloblastic bone marrow, was found to have sickle-cell anemia in addition to pernicious anemia. In vitro sickling preparations gave positive results, and type AS hemoglobin was shown by paper electrophoresis. The patient responded promptly to therapy with vitamin B_{12} and has been maintained in satisfactory remission for the past three years. As far as can be determined, this combination of findings has not been described previously.

Another patient of interest was a Negro man who was 22 years old when the diagnosis of pernicious anemia was established. His hair, which was quite gray at the time of admission, has gradually returned to its normal color during three years of therapy.

Despite reports in the literature of a high incidence of gallbladder dysfunction and of cholelithiasis[9,10] in association with pernicious anemia, only one patient in this series had complaints referable to the biliary tract. This subject was found to have a solitary ball-valve stone of the pigment type, which produced intermittent upper abdominal pain and typical Charcot's intermittent fever. Diagnosis and correction of this condition were delayed by the fact that reflux of barium from the duodenum into the enormously dilated common bile duct radiologically simulated a duodenal diverticulum, and the surgical service was reluctant to operate.

Macrocytic Anemia Due to Gastrectomy

Three patients in this series had undergone total or subtotal gastrectomy prior to the onset of macrocytic anemia. In our opinion, the occurrence of deficiency in intrinsic factor as a result of subtotal gastrectomy has not been emphasized sufficiently. One of our patients was 56 years old at the time that a gastrojejunostomy was performed in 1947 for relief of pyloric obstruction resulting from a duodenal ulcer of 20 years' duration. Persistence of symptoms, with two episodes of hemorrhage from the upper gastrointestinal tract, led to the diagnosis of a marginal ulcer in 1952. Subtotal gastrectomy was performed at that time. A macrocytic anemia was demonstrated first in 1954. The patient did not cooperate in his therapy and at the time the Schilling test was performed in 1957 he was found again to have a moderately severe macrocytic anemia. With the Schilling test, vitamin B_{12} excretion was 2 per cent when the vitamin was given alone and 14 per cent after the administration of vitamin B_{12} and intrinsic factor. Administration of vitamin B_{12} did not produce a satisfactory increase in erythrocytes. The mean corpuscular volume decreased from 101 to 78 μ^3, and a diagnosis of dimorphous anemia was made. Iron deficiency appeared to be the secondary factor limiting response to therapy. This was confirmed by finding a low concentration of iron in the serum. Ferrous gluconate tablets were added to the regimen but had no effect on the anemia, and serum iron concentration remained low. An orally given iron tolerance test was performed with elixir of ferrous gluconate, and normal absorption was demonstrated with this form of iron. When the elixir was substituted for tablets in this patient's therapeutic regimen, the blood count returned to normal.

Another patient, who was a chronic alcoholic, had a subtotal gastrectomy performed

14 years before he was admitted in 1956 with a macrocytic anemia of moderate degree. The bone marrow was normoblastic and achlorhydria was noted on gastric analysis. Results of the Schilling test were 3.6 per cent excretion of vitamin B_{12}-Co^{60} after administration of the vitamin alone and 10.1 per cent after administration of vitamin B_{12} and intrinsic factor concentrate. The Schilling test was followed by improvement in the peripheral blood picture. The patient failed to return for follow-up examinations and died in January 1957.

The third patient was 39 years old at the time that total gastrectomy was performed in 1940. The postoperative diagnosis was linitis plastica of syphilitic origin. A gumma of the left lobe of the liver also was removed during the operative procedure. One year following surgery, a macrocytic anemia developed which responded well to the administration of liver extract. Therapy was interrupted in 1946, and in 1947 the patient came to the clinic complaining of weakness, dyspnea and paresthesias of the hands and feet. Examination of the peripheral blood revealed a moderately severe macrocytic anemia. On administration of folic acid, the patient improved considerably. Vitamin B_{12} was added to the therapeutic regimen in 1948. When the Schilling test was performed in 1956, the patient was asymptomatic and the peripheral blood picture was normal. The Schilling test showed 0.2 per cent excretion following administration of vitamin B_{12} alone and 16.4 per cent after administration of vitamin B_{12} and intrinsic factor.

It is interesting to note that the results obtained with the Schilling test when vitamin B_{12}-Co^{60} was given alone were definitely better in the two patients who had had subtotal gastrectomy than in the patient who had had total gastrectomy. Excretion was also higher than in patients with true pernicious anemia, with two exceptions. Of the 42 patients in this latter group, values in excess of 1 per cent excretion were found in only eight subjects. Two of these, a white man and a Negro man, had values greater than 2 per cent (3.3 and 2.8 per cent, respectively).

Therapy of Pernicious Anemia

All but three of the patients studied in this series were treated with large doses of orally administered crystalline vitamin B_{12} at weekly intervals as part of another study. They have been maintained in satisfactory remission for periods as long as eight and one-half years with orally given doses of the vitamin ranging from 1000 to 3000 μg. once a week. Excellent response was obtained in 24 subjects who received vitamin B_{12} orally as initial therapy. Findings in some of these subjects were included in a report published previously.[11] All patients, of course, received parenterally administered vitamin B_{12} as part of the Schilling test; for some of the patients, this constituted initial therapy. Others received liver extract parenterally, vitamin B_{12} intramuscularly, or orally administered preparations containing a combination of vitamin B_{12} and intrinsic factor as initial treatment before they were referred to us.

It should be emphasized that therapy with large, orally given doses of vitamin B_{12} is not accepted generally as a method of treating pernicious anemia, although, in our experience and in that of others, it has proved to be satisfactory in most instances.[11] Doses of the size employed in our study are apparently absorbed by simple diffusion through the intestinal mucosa without the aid of intrinsic factor. The orally administered regimen has the advantages of flexibility, ease of administration, and potentially lower cost in comparison with parenterally given crystalline vitamin B_{12} or orally administered preparations containing vitamin B_{12} and intrinsic factor. The last-mentioned preparations are difficult to standardize and are not uniformly satisfactory.

The plan of treatment which we recommend for general use is one which we have employed successfully for many years in another group of patients not included in this series. Initial therapy consists of intramuscular administration of 50 μg. of crystalline vitamin B_{12} three times weekly for two weeks, followed by 100 μg. intramuscularly at intervals of four weeks. This treatment must be continued for life, and adequacy of the patient's response should

be checked frequently. A complete blood count and neurologic examination will indicate whether or not therapy is satisfactory. Occasionally, a patient may be encountered in whom this dosage is not sufficient for maximal benefit. The variation among individuals in therapeutic requirements of vitamin B_{12} makes it mandatory to determine the optimal regimen for each patient.

The hazards of inadequate or delayed therapy in patients with pernicious anemia have been discussed previously. Multivitamin preparations, which are available without prescription, may contain sufficient quantities of folic acid to bring about hematologic response in patients with pernicious anemia without preventing the development of lesions of the central nervous system. Use of these preparations may mask the characteristic blood and bone-marrow changes of pernicious anemia and lead to confusion and delay in diagnosis with progression of neurologic disease to an irreversible stage.

Role of Intrinsic Factor in Vitamin B_{12} Metabolism

It has been recognized for many years that failure of the stomach to elaborate intrinsic factor is the etiologic basis of pernicious anemia. Extensive investigation has been undertaken to isolate and characterize intrinsic factor but the chemical composition remains unknown, although material active in amounts of less than 1 mg. have been obtained. Intrinsic factor is necessary for the absorption of vitamin B_{12} from the intestinal tract in the small quantities present in the average diet. Diets high in animal protein may contain sufficiently large amounts of vitamin B_{12} so that some will be absorbed in the absence of intrinsic factor, probably by simple diffusion. Using an in vitro test for intrinsic factor activity, we have found small quantities in the gastric juice of some patients with pernicious anemia.[12] While these tests do not have absolute specificity, it seems likely that some patients with pernicious anemia elaborate some intrinsic factor and others none, which may partially account for variation in therapeutic requirements for vitamin B_{12}. It is known that without treatment some patients may remain in remission for longer periods than others.

Experiments in our laboratory indicate a role for intrinsic factor in addition to facilitating absorption of vitamin B_{12}. Intrinsic factor has been found to increase the ability of certain proteins in serum and in many tissues of the body to combine with vitamin B_{12}.[13] The interaction of vitamin B_{12}, intrinsic factor and receptor protein requires a cofactor which appears to be ribonucleic acid.[14] Considerable evidence suggests that intrinsic factor is absorbed into the circulation and that it also is absorbed into the cells of the liver and presumably into cells of other organs as well.[15] Most of the vitamin B_{12} in serum is bound to protein. The amount of bound vitamin B_{12} in serum is less in patients with pernicious anemia than in normal subjects, even after administration of massive doses of vitamin B_{12}.[16] Perhaps this is due to lack of intrinsic factor in the serum in pernicious anemia. The interaction of vitamin B_{12}, intrinsic factor and receptor proteins of various tissues, which has been demonstrated in vitro, suggests that intrinsic factor may assist in vivo in the storage of vitamin B_{12} in the liver and other tissues. In the light of present knowledge, it is our opinion that intrinsic factor may be considered a hormone which is elaborated by the stomach and exerts important regulatory effects on vitamin B_{12} metabolism. In all likelihood, the role of intrinsic factor will not be delineated completely until chemical characterization of this substance has been achieved.

Summary

The clinical and laboratory findings in 45 patients in whom the diagnosis of pernicious anemia was confirmed by the Schilling test are reported. Pernicious anemia was found to be more common in the Negro than has been reported previously. The occurrence of pernicious anemia after subtotal as well as total gastrectomy was pointed out. Difficulties in the diagnosis of pernicious anemia were illustrated by problems encountered in this group of patients. Consideration also was

given to some of the medical conditions which may be found in association with this disease. The therapy of pernicious anemia with orally and parenterally administered preparations of vitamin B_{12} was discussed and the neurologic hazards of delay in diagnosis and in institution of treatment were emphasized. Certain concepts of the role of intrinsic factor in vitamin B_{12} metabolism were presented.

The Schilling test has proved to be a useful procedure in differentiating pernicious anemia from other syndromes in which macrocytic anemia or malabsorption of vitamin B_{12} is observed.

ACKNOWLEDGMENTS

The authors wish to express their appreciation to Mrs. Jean Snider for technical assistance in these studies.

The vitamin B_{12}-Co^{60} used in the Schilling test was provided through the courtesy of Dr. Nathaniel S. Ritter, Merck Sharp and Dohme, Division of Merck & Co., Inc. Dr. Ritter also provided the preparation of vitamin B_{12} which was used in treating these patients. Intrinsic factor concentrate was supplied by Mr. Robert Jones, Abbott Laboratories.

REFERENCES

1. Schilling, R. F.: Intrinsic factor studies. II. The effect of gastric juice on the urinary excretion of radioactivity after the oral administration of radioactive vitamin B_{12}. J. Lab. & Clin. Med. 42:860, 1953.
2. Goldsmith, G. A., Hunter, F. M., Prevatt, A. L. and Unglaub, W. G.: Vitamin B_{12} and the malabsorption syndrome. Am. J. Gastroent. 32:453, 1959.
3. Rosenthal, H. L. and Sarett, H. P.: The determination of vitamin B_{12} activity in human serum. J. Biol. Chem. 199:433-442, 1950.
4. Kampmeier, R. H. and Cameron, P. B.: Pernicious anemia in the Negro. Am. J. M. Sc. 192:751, 1936.
5. Schwartz, S. O. and Gore, M.: Pernicious anemia in Negroes. Arch. Int. Med. 72:782, 1943.
6. Wintrobe, M. M.: Clinical Hematology. Ed. 4. Philadelphia, Lea & Febiger, 1956.
7. Riddle, M. C.: The endogenous uric acid metabolism in pernicious anemia. J. Clin. Invest. 8:69-88, 1929.
8. Sears, W. G.: Occurrence of gout during treatment of pernicious anemia. Lancet 1:24, 1933.
9. Boyden, E. A. and Layne, J. A.: The gall bladder in patients with pernicious anemia; a study of nonvisualization and rate of emptying. Gastroenterology 4:121, 1945.
10. Bethell, F. H. and Harrington, B. D.: Incidence and significance of disease of gall bladder and liver in pernicious anemia. Am. J. Digest. Dis. 1:256, 1934.
11. Unglaub, W. G. and Goldsmith, G. A.: Oral vitamin B_{12} in the treatment of macrocytic anemias. South. M. J. 48:261-269 (March) 1955.
12. Goldsmith, G. A.: Nutritional anemias with especial reference to vitamin B_{12}. Am. J. Med. 25:680-689 (November) 1958.
13. Miller, O. N. and Hunter, F. M.: Effect of intrinsic factor concentrates on vitamin B_{12} receptor protein of tissues. Proc. Soc. Exper. Biol. & Med. 97:863-867, 1958.
14. Hansen, H. J. and Miller, O. N.: On the interaction of intrinsic factor and cofactor. (Abstr.) Fed. Proc. 19:418, 1960.
15. Miller, O. N., Hansen, H. J. and Troncale, F. J.: Further studies on the absorption of intrinsic factor. (Abstr.) *Ibid.*[14]
16. Unglaub, W. G., Miller, O. N. and Goldsmith, G. A.: "Saturation" studies with vitamin B_{12} in human subjects. Am. J. Clin. Nutrition 6:535-541 (September-October) 1958.

CLINICAL STUDY

Clinical Evaluation of Fluphenazine in Cases of Anxiety and Other Psychoneuroses

TIBOR BODI, JOHN H. NODINE, PETER E. SIEGLER, HOWARD A. LEVY AND JOHN H. MOYER*

Hahnemann Medical College and Hospital, Philadelphia

Halogen substitution and introduction of a piperazine ring into the side chain of the chlorpromazine molecule resulted in a compound which is effective in small doses and thus appears to have reduced hypnotic potential and neurotoxicity.

Clinical studies indicate that fluphenazine produced clinically satisfactory improvement in the majority of patients suffering predominantly from anxiety; most of them were treated with only 0.5 mg. or less per day. Studies so far revealed minimal incidence of side effects.

Fluphenazine seems to be a potent psychopharmacologic agent in the clinic or office management of anxiety states and other psychoneuroses.

MODIFICATIONS of the chlorpromazine molecule have been effected in an attempt to reduce unpleasant side effects. Halogen substitution and introduction of a piperazine ring into the side chain of the chlorpromazine molecule have yielded compounds which are effective in small doses and thus have reduced hypnotic potential and neurotoxicity.[1-4] Fluphenazine, a new trifluoromethyl homolog of perphenazine, is such a drug; the complete chemical formula is 4-{3[2-(trifluoromethyl)-10-phenothiazinyl]propyl}-1-piperazineethanol dihydrochloride, and its structure is shown in figure 1.

TIBOR BODI

Fluphenazine induced signs of motor and sensory depression following each daily dose in monkeys. The drug was reported to be 25 times as potent as chlorpromazine, as indicated by relative suppressive potency in the conditioned avoidance behavior in animals. The drug showed no significant toxicity in animals.[5] In addition, no significant endocrine effects were shown.

This drug was found to be effective in most of the psychoses[3,6] and also in psychoneuroses.[7]

*Department of Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania.

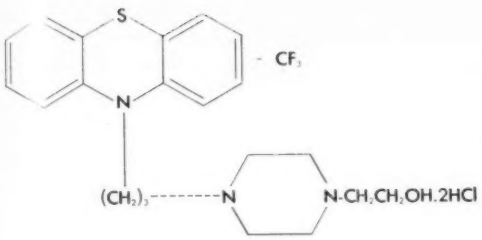


FIGURE 1. Structural formula of fluphenazine.

Preliminary observations seemed to indicate that fluphenazine would be beneficial in psychoneurosis when only a small dose was given once a day. Therefore, the purpose of this study was to investigate short-term effectiveness of this new compound in ambulatory patients with anxiety reaction when either a daily single dose or small divided doses are administered.

Material and Methods

Forty patients with psychologic problems were selected from the general medical clinic of Hahnemann Hospital. Thirty-seven patients were available for follow-up. Three patients failed to return for unknown reasons. This is not considered unusual with this type of patient. Of the 37, there were six men and 31 women, of whom 23 were Negroes and 14 were whites, with an age range from 18 to 67 years and a mean age of 42.8 years. In some of the patients, the anxiety reaction was secondary to somatic disease. They were given a thorough medical evaluation with laboratory studies, including chest x-rays, complete blood cell counts, urinalyses, serologic tests, and special tests or consultations when indicated. Patients were referred to the special medical clinic and followed by a psychopharmacologic team of internists, psychologists, a psychiatrist and a social worker. During the course of drug therapy, the patients were evaluated at weekly or biweekly intervals.

The initial dosage was 0.1 mg. fluphenazine twice daily. This was successively increased at weekly or biweekly intervals to 0.25 mg. twice daily. Thereafter, 0.5 mg. of the drug was given as a single early morning dose. This dosage was maintained whenever possible. If the result was not satisfactory, the dosage was increased to 0.5 mg. twice or three times daily. We were interested only in using the outlined low-dosage schedules; therefore, no attempt was made to increase the dose further or to push it to the maximal dose that could be tolerated in the respective cases. A placebo or phenobarbital was frequently substituted for similar periods of time, or repeated when the therapeutic effect was uncertain.

The criteria for evaluating response to treatment were based on both subjective statements and clinical observation of the patients at consecutive interviews. When improvement was questionable, no improvement was recorded on the chart and the drug-response cards. Slight improvement consisted of little more than partial relief of the patient's complaints. Moderate improvement meant that the patient had considerable relief of complaints, and marked improvement meant that the patient became essentially asymptomatic during drug treatment. Stereotyped questions were avoided in order to prevent influencing the patient by suggestion, and psychotherapy was restricted to the usual reassurance necessary to have the patient take the medicine and follow through with the study. Periodic blood cell counts, urinalyses, and liver function studies were performed in the clinical pharmacology-toxicology laboratory with specimens collected by a technician stationed in the special medical clinic during each clinic session.

Results

The 37 patients received fluphenazine for a total of 1,858 days, an average period of administration of 50.2 days. The clinical response to therapy is summarized in table 1. Definite improvements in the psychologic symptoms occurred in 31 of the 37 patients (84 per cent), including those in the slightly improved category. Placebo administration to 19 of these patients resulted in improvement in 10 patients (53 per cent). Details are shown in table 2. Statistical analysis of this difference in individual response to drug and placebo showed that one patient responded to both the drug and the placebo, and four patients

TABLE 1

SUMMARY OF THERAPEUTIC RESPONSE TO FLUPHENAZINE

DIAGNOSIS	NUMBER OF PATIENTS	RESPONSE			
		None	*Slight*	*Moderate*	*Marked*
Anxiety reaction*	20	3	3	11	3
Psychoneurosis (other than anxiety)	9	1		4	4
Psychophysiologic reaction	2	2			
Personality disorder	3		1		2
Schizophrenic reaction	2			1	1
Adjustment reaction of late life	1			1	
TOTAL	37 (100%)	6 (16%)	4 (11%)	17 (46%)	10 (27%)

*In 13 of these patients, anxiety reaction was secondary to somatic disease.

TABLE 2

SUMMARY OF RESPONSE TO PLACEBO

DIAGNOSIS	NUMBER OF PATIENTS	RESPONSE†		
		None	*Slight*	*Moderate*
Anxiety reaction*	7	4	2	1
Psychoneurosis (other than anxiety)	7	3	4	
Psychophysiologic reaction	1		1	
Depressive reaction	1			1
Adult situational reaction	1	1		
Schizophrenic reaction	1	1		
Adjustment reaction of late life	1		1	
TOTAL	19 (100%)	9 (47%)	8 (42%)	2 (11%)

*In five patients, anxiety reaction was secondary to somatic disease.

†None of the patients showed marked response.

responded to neither of them. Omitting those who did not respond to the placebo or the drug or responded to both, the ratio between those with satisfactory response to the drug only and placebo only is 13:1, respectively. This is highly significant, with a correlation coefficient of less than 0.01. The degree of improvement observed in the patients receiving fluphenazine was also of interest, as 10 patients (27 per cent) became practically asymptomatic and an additional 17 (46 per cent) were moderately improved. Thus, satisfactory clinical response was found in a total of 73 per cent of patients and was generally characterized by relief of anxiety, relaxation, elevation of mood, and less disturbance with the underlying somatic disease, if present. Although patients with anxiety, who made up half of our group, were impressively relieved of their symptoms, improvement was distributed through the various diagnostic categories. The drug seemed to have had a beneficial effect in two patients later diagnosed as schizophrenics.

TABLE 3

OPTIMAL THERAPEUTIC RESPONSE TO FLUPHENAZINE WITH VARIOUS DOSAGE SCHEDULES

DOSAGE (MG.)	NUMBER OF PATIENTS*	RESPONSE		
		Slight	*Moderate*	*Marked*
0.15 t.i.d. (0.45)	1		1	
0.25 b.i.d. (0.5)	8	1	2	5
0.5 q.d. (0.5)	10	2	5	3
0.15 q.i.d. (0.6)	1		1	
0.25 t.i.d. (0.75)	2		2	
0.5 A.M. and 0.25 P.M. (0.75)	1		1	
0.5 b.i.d. (1.0)	7	1	4	2
0.5 t.i.d. (1.5)	1		1	
TOTAL	31 (100%)	4 (13%)	17 (55%)	10 (32%)

*Six patients who received no benefit from therapy were excluded.

The optimal dose schedules of fluphenazine and the therapeutic response with our limited dosage in the 31 patients are summarized in table 3. Six patients showing no appreciable improvement on our dose schedule were omitted in this table. A single early morning dose of 0.5 mg. of fluphenazine induced moderate or marked response (clinically satisfactory improvement) in 8 of the 10 patients. Similar results were obtained in seven of the eight patients by giving 0.25 mg. twice daily. In six of seven patients, the clinically satisfactory response was reached after 0.5 mg. was given twice daily. Only one patient required 0.5 mg. three times daily. Five patients required an individualized dosage, varying between 0.45 and 0.75 mg. daily. Therefore, 15 of the 31 patients had good control of anxiety or other psychologic symptoms with 0.5 mg. fluphenazine daily in a single or divided dose; the dosage for the remaining 16 had to be individualized, with 12 patients showing satisfactory clinical improvement.

The side effects and dosage levels at which they occurred are presented in table 4. The most common side effect, mild drowsiness (often associated with dizziness and apathy), occurred in three patients. It did not necessitate cessation of therapy. One of these patients experienced a "falling down" sensation consistent with mild equilibrium disturbance. Two patients receiving 0.25 mg. of fluphenazine twice and three times daily, respectively, became restless at night. Omission of the evening dose remedied this situation. One patient became lightheaded, which suggested neurocirculatory imbalance. One patient experienced red blotches over the body and extremities after one week of therapy with 0.1

TABLE 4

SIDE EFFECTS WHILE ON FLUPHENAZINE

SIDE EFFECTS	NUMBER OF PATIENTS	DAILY DOSE (MG.)
Urticaria	1	0.4
Apathy, drowsiness, mild akinesia	1	0.5
Neurocirculatory imbalance, mild	1	0.5
Insomnia, apathy	1	0.5
Leukopenia, transient	1	0.5
Akinesia, mild	3	0.5 (2 patients); 0.6 (1 patient)
Drowsiness, dizziness, "falling down" sensation, insomnia	1	0.75
Drowsiness, dizziness, apathy	1	0.75

mg. of fluphenazine four times daily. The rash disappeared in one week after discontinuation of the drug. A single white blood cell count of 3300 per cubic millimeter (54 per cent polymorphonuclear leukocytes) was reported for one patient, but repeated counts, each made in triplicate, one week later were normal even with continuation of the therapy.

None of these side effects except the urticaria interfered with the therapy, nor did they cause serious or permanent sequelae. In four patients, there appeared to be some decrease in the daily activity, which was characterized by a tired, "empty-headed," lazy sensation, associated with mild drowsiness. This was thought to be related to the mild akinetic effect of the drug rather than to actual psychic inertia of the patients. Although the patients were carefully observed for signs of akathisia (motor restlessness), it did not appear during our low-dosage therapy. The insomnia reported was really night restlessness and could not definitely be attributed to the drug.

The side effects occurred between the dosage range of 0.4 and 0.75 mg. per 24 hours, showing no definite relationship to the limited dosage administered in this study. Tolerance to fluphenazine was not noted in any of these patients during the period of therapy. There were two cases in which the initial good response was lost. Situational stress and exacerbation of an organic disease in one of these patients accompanied the transient poor response. The other patient had an irritated colon. Three illustrative case reports follow.

Case Reports

Case 1—A 42 year old divorced Negro housewife was first seen in the medical clinic of Hahnemann Hospital in 1954 because of epigastric pain which was relieved by alkali. Subsequent x-ray examination revealed a deformed duodenal bulb, and a diagnosis of duodenal ulcer was made. The intermittent ulcer symptoms were fairly well controlled with standard therapy; however, severe anxiety pertaining to her illness gradually developed. She began to have pains, numbness in the calves of the legs, apathy, apprehension, a quivering feeling in the stomach, and flatulence, which were not alleviated by therapy. The patient was under stress. She lived in a noisy apartment in midcity, and was worried about being separated from her husband and raising four children, one of whom was an epileptic. She had a chronic anxiety reaction with conversion features secondary to duodenal ulcer. Administration of 0.1 mg. fluphenazine three times daily in addition to a diet regimen for ulcers gave prompt relief of pain and a definite amelioration of anxiety and functional colonopathy. The dosage of fluphenazine was increased to 0.25 mg. twice daily with a continuation of the good clinical effect. She remained on this dosage and the ulcer diet for the next three months and continued to be relatively free of symptoms. Then a placebo was substituted for the fluphenazine, and within two weeks anxiety and functional gastrointestinal disturbance recurred, necessitating reinstitution of ataractic therapy.

Case 2—A 52 year old white housewife began to have asthmatic attacks in 1946. The asthma became worse, especially during the summer and when she was emotionally upset. During the court procedure for separation from her husband, status asthmaticus developed. Intensive therapy in the allergy clinic was not effective. She broke down into crying spells following any questioning. She stated that she was put out of the house by her husband and left penniless after 25 years of marriage. It was obvious that the gross stress situation precipitated the status asthmaticus and the acute anxiety state with hysteric components. Treatment with 0.5 mg. fluphenazine twice a day was begun immediately. There was a prompt response during the following week with a decrease of asthmatic attacks. Dosage was decreased and she responded fairly well for a period of one month. However, when the court trial began, a severe relapse in response occurred. The dosage of fluphenazine was increased to 0.75 mg. twice daily. The patient again responded and became calmer, even when she was molested by the divorced husband. She stated that "I was real nervous before but not any more, I am absolutely sure." There was some night restlessness, which is a usual pattern of asthma.

She had been on meprobamate before but preferred fluphenazine since it "helped me more." After the anxiety symptoms subsided, the patient remained on routine therapy for asthma.

Case 3—A 23 year old Greek man came to the United States about two years ago. He was in good health until a year ago when he noticed the onset of a dry cough and irritation in his throat and chest. He was suspected of having bronchitis and subsequently was referred to the medical clinic for evaluation. Here, he underwent a complete physical examination, which included head and chest films, direct laryngoscopy and bronchoscopy. Results of all studies were found to be within normal limits. The patient was then referred to the psychopharmacologic team. He was acutely anxious at this stage and coughed incessantly while being interviewed. He was restless, hostile and bitter about his lack of improvement, for which he blamed his physician. The patient had a domineering mother in Greece, and he was now living in this country with his father who took no active interest in him. He became greatly frustrated working for a "difficult" foreman and developed hostility toward his boss which aggravated his condition. The onset of cough and these environmental changes coincided. The anxiety was so acute that immediate therapy with fluphenazine was started and the patient was referred to the psychiatry clinic. Within a week the patient became much less anxious and could joke during the interview. The cough also became less tormenting. There was an obvious improvement since his first clinic visit. He quit his job, which removed certain stress. He remained on 0.5 mg. fluphenazine at 9 A.M. and 2 P.M. and was referred for vocational guidance to the social service department. Amelioration of this patient's anxiety by the psychiatrist was believed to have been appreciably facilitated by the treatment with fluphenazine.

Discussion

Fluphenazine is a member of the piperazine group of the phenothiazine series. The trifluoromethyl substitution of chlorine and the introduction of a piperazine ring into the side chain of chlorpromazine increased the potency per milligram and reduced the hypnotic and sedative effects and neurotoxicity. Stimulation appeared in an occasional patient on the low-dosage schedule. These properties of fluphenazine contrasted to the marked drowsiness observed in our clinic with a new analog of chlorpromazine where a methylthio group was substituted for chlorine.[8] The hypnotic effect was less pronounced in a methoxy substitute of promazine studied previously.[9]

An evaluation was made of the short-term use of fluphenazine in 37 patients whose chief symptoms were anxiety conversion reactions. The drug seemed quite effective in relieving anxiety. The action was rapid in onset and was prolonged; the side effects were minimal. Temporary drowsiness and dizziness were noted in a few cases, but this is frequently found with such patients, who often complain of these symptoms while receiving no drug or even when given placebo therapy. Night restlessness was not troublesome in our study using a low-dosage schedule. In addition, the drug was not administered in the evening in many instances and the last dose was given at 2 P.M.; however, this was not necessary in all instances. Rudimentary extrapyramidal effects were probably noted once as some heavy sensation in the extremities without actual parkinsonism. Mild akinesia in our group was inferred from symptoms of a few patients who complained of apathy, tiredness or laziness. Except for one patient with urticaria, the drug was taken by our patients for an average period of seven and a half weeks. Weight gain of no more than 2 to 3 lb. was noted in a number of these patients. Polyphagia and menstrual disturbances were not observed in contrast to the effects of chlorpromazine and other phenothiazine derivatives. There was relative freedom from autonomic side effects; in only one instance was there an episode of lightheadedness suggesting neurocirculatory disturbance. This may have been due to the sympatholytic property of the drug.

The single outstanding feature of fluphenazine therapy, according to the members of our psychopharmacology team, was the rapid

alleviation of tension, anxiety and emotional stress—common complaints in the majority of office or clinic patients. When administered in low dosages, the drug seemed to fulfill the criteria of Freyhan[10] by its rapid inhibition of anxiety and psychomotor overactivity. It must be pointed out, however, that until fluphenazine has been further tested over a much more prolonged period, the possibility of hepatic or bone-marrow toxicity must be considered, because it is so closely related to other piperazine derivatives which have caused these reactions.

Summary

Fluphenazine was clinically evaluated in 37 ambulatory patients suffering from psychoneuroses. Clinically satisfactory response was observed in 27 patients or 73 per cent of the group, most of whom were treated with 0.5 mg. or less per day. Placebo therapy in 19 of the 37 patients resulted in some improvement in 10 or 53 per cent, but only two of this group had a clinically satisfactory response. Omitting doubtful reactors, the ratio of those who responded to the drug only to those who responded to the placebo only was 13:1. This is statistically highly significant, with a correlation coefficient of less than 0.01. Hypnotic activity was minimal, requiring discontinuation of therapy or reduction of dose in a few patients only. There were few extrapyramidal signs at our low-dosage schedule, except for mild akinesia in four patients, which did not interfere with the therapy. Fluphenazine seems to be a potent psychopharmacologic agent in the management of clinic or office anxiety states and other psychoneuroses.

No serious toxic effects were observed in this series of patients, but further study is needed to test for possible agranulocytosis and hepatic damage.

ACKNOWLEDGMENT

This study was supported in part by a grant-in-aid from the White Laboratories, Inc., who also supplied the fluphenazine (PERMITIL®).

Technical assistants were Miss Kay Slemmer, B.S., and Misses Marion Beyer and Florence Sprague, who also assisted in administering medication to the patients.

REFERENCES

1. AYD, F. J., JR.: The current status of major tranquilizers. J. M. Soc. New Jersey 57:4-14 (January) 1960.
2. DARLING, H. F.: Fluphenazine: A preliminary study. Dis. Nerv. System 20:167 (April) 1959.
3. AYD, F. J., JR.: Current status of the phenothiazine tranquilizers. Tr. Proc. Acad. Psychosom. Med. 5: 217-221, 1958.
4. ——: Trifluoperazine therapy for everyday psychiatric problems. Current Therap. Res. 1:17, 1959.
5. ROSENKILDE, H. et al.: Fluphenazine—Laboratory and Clinical Data. Bloomfield, New Jersey, Schering Corporation, 1959.
6. AYD, F. J., JR.: Fluphenazine: Its spectrum of therapeutic application and clinical results in psychiatric patients. Current Therap. Res. 1:41, 1959.
7. ERNST, E. M.: Clinical study of fluphenazine in general practice. Clin. Med. 7:1349 (July) 1960.
8. LEVY, H. A., BODI, T., SHARE, I. A. and MOYER, J. H.: A new ataractic compound of the phenothiazine series. Pennsylvania M. J. 62:977-979 (July) 1959.
9. BODI, T., LEVY, H., SHARE, I., NODINE, J. H. and MOYER, J. H.: Methoxypromazine maleate in cases of psychoneurosis. Postgrad. Med. 27:541-547 (April) 1960.
10. FREYHAN, F. A.: Therapeutic implications of differential effects of new phenothiazine compounds. Am. J. Psychiat. 115:577 (January) 1959.

Endocrinology and Metabolism in the University of Washington Teaching Program

ROBERT H. WILLIAMS*

University of Washington School of Medicine, Seattle

ROBERT H. WILLIAMS

WITH the tremendous progress being made in the various specialties of medicine, in order to offer the best training programs it is highly important that material be presented quite systematically and that there be proper coordination of the activities among the specialties. Because the University of Washington School of Medicine is new, these factors were weighed carefully and influenced the physical construction, curriculum, nature of the staff, and many other aspects. Some of these are described in detail herein along with a discussion of other major policies of the School of Medicine and the department of medicine.

The training program described in this manuscript is one of two selected for presentation before the joint meeting (Los Angeles) of the directors of diabetes training programs throughout the United States. Since optimal teaching in diabetes necessitates excellent training throughout the medical school, a major part of the discussion is devoted to policies throughout the University of Washington School of Medicine and the department of medicine in particular.

*Professor and Executive Officer, Department of Medicine, University of Washington School of Medicine, Seattle, Washington.

School of Medicine

Physical facilities—Construction of the School of Medicine of the University of Washington was started only 15 years ago (1946). One mammoth building was designed to house a number of health sciences (figure 1): medicine, public health, dentistry and nursing. Moreover, there are plans for adding wings for pharmacy, biology and genetics. Even now, *all* of the sciences of this large university are adjacent to one another and have close working relationships—an important arrangement since they offer much knowledge and assistance to one another.

In addition to the University Hospital, which is part of the Health Sciences Building, the King County Hospital (520 beds) and the Seattle Veterans Administration Hospital (325

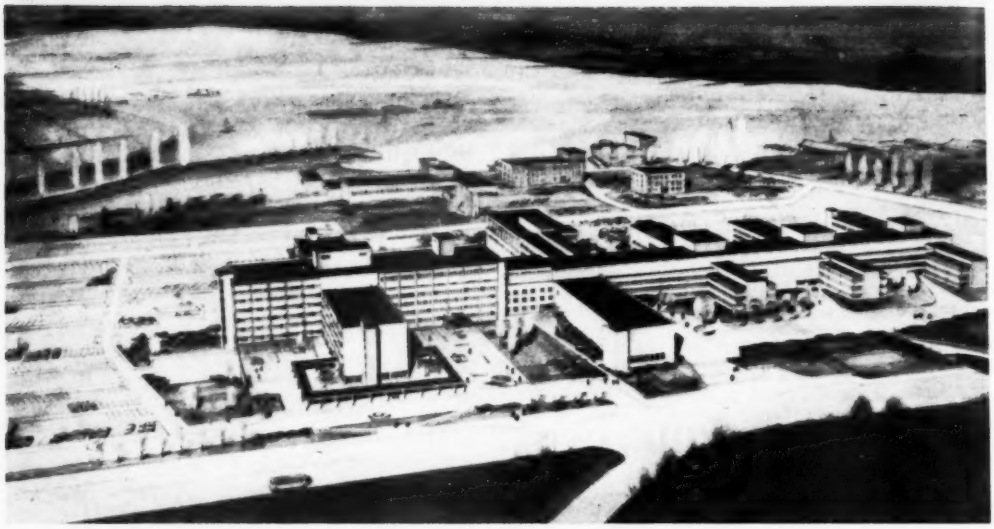


FIGURE 1. Health Sciences Building which houses the University Hospital, clinical sciences, basic medical sciences, dentistry and nursing. In close or immediate proximity are all of the other sciences of the University of Washington. Most of these are not shown in the picture.

beds) are used extensively in the teaching programs. Indeed, from the point of view of teaching, these three hospitals are visualized very much as one, and their teaching activities are carefully coordinated. Although a number of their policies are similar, there are some differences because of differences in patient responsibilities. For brevity, the systems employed at the University Hospital will be presented.

Staff and patient policies at the University Hospital—The major policies are formulated by a hospital executive committee, composed largely of the dean, medical director, hospital administrator and chiefs of the services. Of the hospital's 320 beds, 100 are assigned to the department of medicine. There are 30 beds per nursing unit (ward), most of which are in one or two bed rooms. There are 75 examination rooms in the outpatient unit, all grouped together and designed for coordination of activities of the various clinical departments. There are numerous measures for conserving personnel time, such as different types of conveyer belts, pneumatic tubes, intercommunication systems, a central dictation system, machine accounting and statistics apparatus, and ADDRESSOGRAPH® plates.

This hospital has been built to afford optimal clinical teaching and research. Other functions are subsidiary, but excellent patient care is necessary for the best teaching and research. All patients accepted are used for teaching and are available for research. The patients' financial means range from poverty to millions, but all patients are handled the same in every way, both in the clinic and in the hospital. Indeed, the students, house officers, and even the senior staff often do not know the patient's capacity to pay hospital and professional fees during his management. It is our goal to offer our best to each patient, in both the art and science of medicine, irrespective of how many staff members and departments may be involved. When the problem is clear-cut, major, and confined to one system, the patient is often sent directly to the respective specialist; otherwise, the patient is first seen by internists in the manner that is described later.

"The academic rank and total remuneration of a staff member should be (are) based upon his performance in teaching and research, his duties and responsibilities related to these, and to other activities contributing to the over-all welfare of the Medical School and the University." (Recommendation of the School of Medicine adopted by the board of regents, 1953.) In every way, the staff is encouraged to perform maximally in academic medicine. The lure of pay from paying patients has been inhibited by a system which pools the professional fee income and which places each staff member on a salary.

With the tremendous increase in available laboratory tests, the clinical laboratories have attained a high level of importance in teaching, research and patient care. We have appointed one or more full-time faculty members with major responsibilities in each of the following clinical laboratories: chemistry, microbiology, hematology, electroencephalography and electrocardiography. These staff members are afforded time for their own academic pursuits.

Curriculum studies—Extensive studies of the school's curriculum have been conducted systematically and thoroughly for the last eight years. Complete analyses of the curriculum for each department have been performed by the staff and students. Stringent efforts have been made toward establishing well-defined goals and creating familiarity with the offerings of other departments and toward better coordination and continuity. Increased emphasis has been placed on providing a better environment for learning. Considerable time for elective courses has been offered, along with many good and diversified opportunities for study. Many research fellowships have been offered to students, particularly during the summers. Approximately 100 students engage in research each summer. Approximately 7 per cent of the students withdraw from the medical school curriculum for a year in order to spend additional time in research. During the last two years, a well-organized course dealing with research principles has been provided for research students as well as for research fellows, house officers and others. In this course are presented discussions of general objectives in research, statistical analyses, experimental designs, instrumentation, and critique for reading and writing papers. The Medical Research Society was organized two years ago. Membership is limited to students with demonstrated research ability. Individual student research projects are discussed extensively. By design, almost all of the activities in this society are conducted by the students, with little faculty assistance.

The increased research interests have had a tremendously stimulating effect on the students and have caused them to attain higher goals in many directions.

Basic scientists have had increased participation in third and fourth year teaching, while clinical scientists have increased their teaching in the first two years.

Department of Medicine

With the tremendous progress in medicine, it is not possible for any one physician to master all phases (figure 2). There must be many specialists.[1,2] The efficacy of this plan, as emphasized by Gregg,[3] depends on how smoothly the specialists' activities are coordinated. At the University of Washington we have full-time staff members predominantly engaged in cardiology, endocrinology, neurology, hematology, gastroenterology, dermatology, nephrology, microbiology, rheumatology, allergy and genetics. We need full-time specialists in gerontology, clinical pharmacology, oncology, nutrition, respirology and other specialties, including many additional general internists.

Each specialty is set up as a division of the department of medicine and is accorded considerable freedom with respect to research, teaching, administration and patient care. However, there is significant integration in the last three activities, and many common patterns are followed. The divisions are dealt with reasonably equitably with respect to budget, space, personnel, curriculum allocations, etc. There is considerable coordination of activities with other departments, including teaching exercises.

Patients prejudged as having a single, clear-cut disorder are usually referred directly to a specialty clinic (figure 3); otherwise they are handled in the group clinic (general medical clinic). In either instance there are a complete history, physical examination, and routine laboratory work. Most new patients are assigned to fourth year students, who present the cases in detail to selected faculty; the discussions are relatively extensive. Residents and research fellows assist with various phases of patient care, but are not given the major responsibility for teaching. Actually, there is a "team" approach, with all of these groups proceeding together, following systems which stimulate everyone to think extensively. Each student keeps his own patient appointment book, and efforts are made to encourage his following the patients as much as possible.

The group clinic is one staffed by general internists as well as by specialists in different phases of medicine. Periodically, a few senior staff members from other departments are called to the clinic area for brief consultations. Such accommodations are often easy because specialists in other departments work in clinics only a few feet away. The student who previously examined the patient presents the data, irrespective of who the specialist is. Moreover, when the patient is referred to one of the specialty clinics in medicine, the student often follows the patient to that clinic and continues to play a role in his management. We have two excellent young internists who together give full-time coverage in coordinating smoothly the activities of the clinics in medicine with one another and with those of other departments.

For a while we encountered a number of major problems in dealing with inpatients, resulting chiefly from lack of proper coordination and definition of responsibilities. Such patients serve in the education of many groups: students, interns, residents, research fellows, faculty, postgraduate students and others. Moreover, some patients serve as excellent subjects for clinical investigations. With the many different objectives and individuals involved, it is easy for confusion to develop. However, we have found that a great improvement resulted from the following scheme: Each ward has a chief ward physician, assigned for intervals of two or three months. He spends two to three hours a day, seven days a week, on "ward rounds." He has the responsibility for the entire ward and sees to it that *all* of the interests are properly coordinated (figure 4) and that the patient is cared for in the most efficient manner.

We also make use of many specialists, but their activities are coordinated and their responsibilities designated in each case and made clear to everyone on the ward, including the patient and his referring physician.

We encourage a minimum of three years of training as a house officer, irrespective of whether the resident plans an academic career or private practice, and irrespective of whether he intends to confine himself chiefly to a specialty in medicine. We also encourage him to spend two years as a research fellow, preferably following house officer training, whether or not he will engage in an academic career or in practice.[4] We have about 40 residents in our integrated residency program in medicine and 30 research fellows. In addition to offering extensive individual instruction for the research fellows, we offer systematic courses in research, its philosophy, objectives, experimental designs, methodology, instrumentation, biometrics and various other specialties. The research fellows regularly conduct their own meetings, at which time they discuss research activities of the various divisions of medicine.

*Division of Endocrinology and Metabolism**

For optimal understanding of the problems of diabetes, a broad training in basic sciences as well as clinical sciences is indicated. The disease involves major disturbances in the metabolism of carbohydrates, fats, proteins, minerals and water, and it can be asso-

*The author is the director of the training program in these fields at the University Hospital, while Dr. John Bakke is director at the Veterans Hospital, and Dr. Alvin Paulsen at the King County Hospital, but these activities are extensively coordinated. Likewise, there is increasing coordination of the activities with other departments.

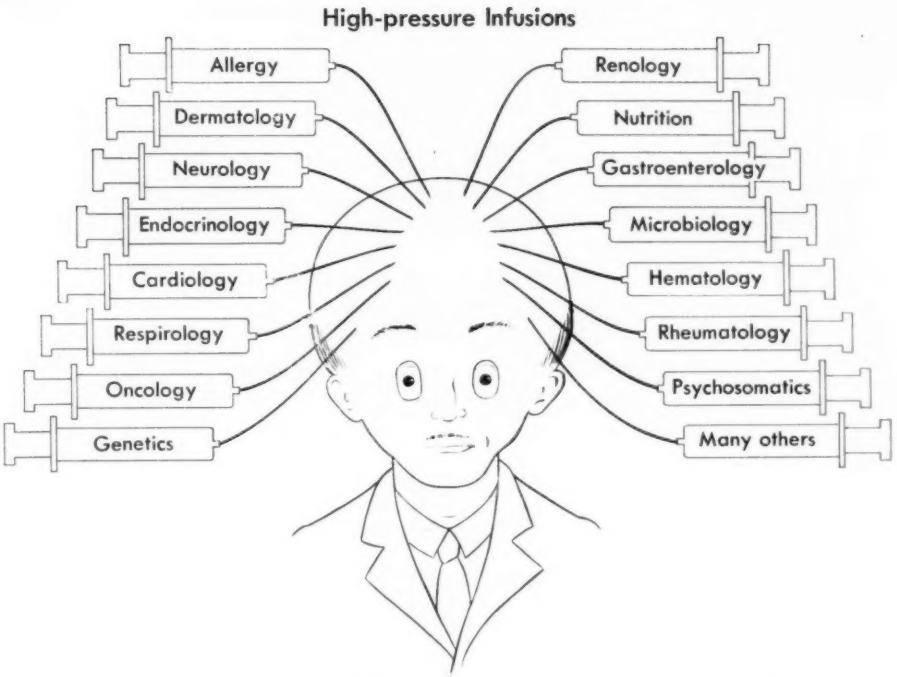


FIGURE 2. Full load of knowledge of all medical specialties—too much for any one physician.

(Figures 2 to 4 reproduced courtesy J.A.M.A.[3])

ciated with abnormalities in function in essentially every anatomic system. There are few diseases that cannot influence its course. Its complications involve the heart, brain, nerves, eyes, kidneys and other sites.

It is possible to stimulate great interest by revealing the considerable strides that have been made in the understanding of the metabolism of carbohydrates, fats and proteins, the role of oral hypoglycemic agents, and other areas. A very important point is that the extent to which the trainee becomes interested frequently depends on the personal relationships developed between individual faculty members and the trainee. With the heavy load carried by many staff members and the division of responsibility among many specialists, the trainee not uncommonly believes that none of his instructors are interested in him as an individual. Informal contacts at "coffee," lunch, supper, or at other times help in this regard—indeed, they sometimes have an enormous influence on the trainee's entire career.

Many full-time and part-time staff members whose main specialty is in endocrinology and metabolism engage in the teaching program. These consist of representatives from the majority of the clinical and basic medical science departments.

I have on several occasions invited all who were interested from each department to discuss the teaching in endocrinology. I conducted a systematic survey of the objectives of each department and of what was being taught. Particularly in the last year all departments have made a greater effort to (1) avoid unnecessary duplication, (2) improve their integration, and (3) increase the conjoint teaching exercises.

Students (70 per class), interns and residents (75), research fellows (4), and postgraduates (hundreds) are taught. Much of the training program for each of these differs.

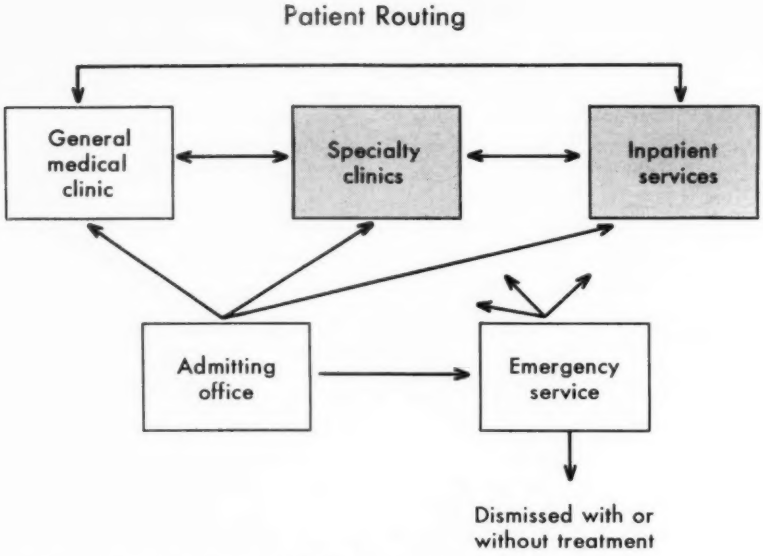


FIGURE 3. Appropriate routing of patients is highly important in saving unnecessary expense and loss of time by patients, staff and students and in improving both teaching and patient care.

There are several weekly seminars in endocrinology and metabolism, ward rounds, and clinics. They cover all phases of endocrinology, intermediary metabolism, water and electrolyte balance, etc.

In the first and second medical school years, only about 10 hours of the time allotted to internal medicine are spent in endocrinology, except in the laboratory diagnosis course, which includes approximately 12 hours. In the second year, however, a 40 hour elective course in endocrinology is offered. This specialty course is elected more than any other: 65 per cent of the class took it in the first quarter and 30 per cent in the second quarter.

The research fellows constitute a very important group, because they will be the future leaders in endocrinology and metabolism, both in clinical practice and in academic medicine. The usual number is four and the period of training, two years. When their training is completed, the fellows have seen a broad spectrum of endocrine and metabolic problems and are familiar with the most significant clinical endocrine tests. They also learn many general principles of research as well as methodology along specific lines. A full-time biochemist is of enormous help in familiarizing the fellows with experimental design, instrumentation, methodology, biometrics, critical analysis of literature, paper writing, etc. The fellows are encouraged to investigate some of their own interests independently, but they are afforded considerable assistance by senior members. The fellows have weekly formal conferences relative to their research and have informal discussions very frequently. They spend the majority of their time with research, which varies from highly basic laboratory investigation to clinical studies. The fellows see all of the consultations in endocrinology, before the senior staff. These comprise a large volume and excellent variety of endocrine and metabolic problems. Endocrine ward rounds are conducted several times weekly. The fellows work one day each week in the endocrine and diabetes clinic at the King County Hospital and spend the same amount of time in the endocrine clinic at the University Hospital. Moreover, as indicated earlier, they attend several weekly conferences in endocrinology and metabolism.

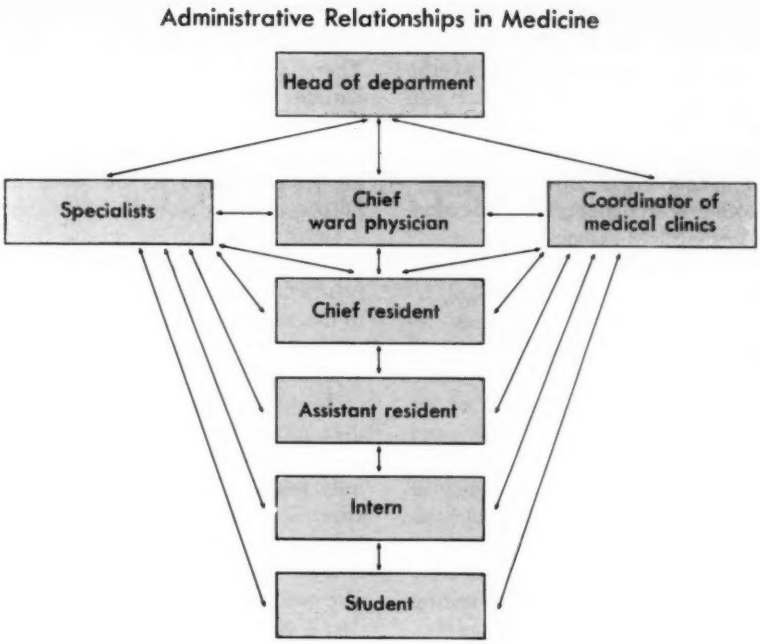


FIGURE 4. Proper coordination in teaching, research and patient care is imperative in a training program. The chief ward physician is responsible for coordinating ward activities with those of the general medical and medical specialties clinics. He must work closely with the coordinator of medical clinics as well as with other staff members involved. The medical director is coordinator of interdepartmental activities.

Summary and Conclusions

Diabetes is associated with extensive and diversified metabolic disorders manifested in many different systems in the body, and its course may be modified by a large number of factors. The acquisition and understanding of the available knowledge relative to this disease, along with many other diseases, is a mammoth task. Some aids toward optimal accomplishments consist of: (1) careful studies of the entire medical school curriculum and the application of appropriate modifications, (2) the provision of a desirable number and type of patients, (3) the procurement of sufficient staff with proved excellence in teaching, and (4) the provision of adequate research opportunities for students and graduates.

During the past eight years we have conducted at the University of Washington extensive studies of the medical school curriculum, as well as that of schools elsewhere. The curriculum here has been evaluated thoroughly by students, house officers, faculty and others. Indeed, thousands of hours have been spent in scheduled discussions of the curriculum and its modifications. Some of the more prominent general conclusions follow: There must be increased effort to (1) define the goals and make them known to the faculty, students and others, (2) become acquainted with what is taught by other divisions and departments, and (3) increase the coordination and collaboration in teaching, with better interdigitation with respect to content and the time of presentations.

We have greatly increased the amount of vertical teaching. For example, there is increased collaboration in planning and in conjoint teaching by staff endocrinologists in various basic science and clinical science de-

partments. The training of students, residents and research fellows in our three teaching hospitals is carefully integrated. *All* of the sciences at the University of Washington are grouped together physically; all of the health sciences, including the University Hospital, are in one building. This physical arrangement has promoted collaboration and coordination in teaching and research.

In view of the tremendous progress in medicine, with the necessity of frequently acquiring new concepts or modifying old ones, we have attempted to stimulate initiative, originality, independence and creativeness. We have encouraged the acquisition of good broad approaches in working out new concepts and in establishing their validity. Such training, of course, has emphasized the importance of training in research. Therefore, we have offered formal courses dealing with general principles in research: philosophy, experimental design, biometrics, reading and writing papers, etc. We also have offered specific courses in methodology and in individual sciences. A good supply of research fellowships and encouragement from the faculty have helped induce about 100 students to spend their summers in research and 5 to 10 per cent to withdraw from their standard curriculum to spend a year or more. The students have recently started a medical research society which meets about 20 times annually for the presentation and extensive discussion of their research.

There are 30 graduate research fellows in the department of medicine, five of them in endocrinology and metabolism. This group is offered formal courses in research, as well as extensive individual training in fundamental laboratory research and in clinical research. Six biochemists who are employed full time in the department of medicine have been of enormous aid in this training program.

The full-time staff is, indeed, full time. There are no "private" patients seen. The patients admitted to the University Hospital span the financial spectrum, but teaching and research are the primary aims and no patients are admitted who are not available for those purposes. All are handled in a similar manner —same staff, waiting space, hospital rooms, etc. The staff's total remuneration is essentially a salary which is not particularly related to the number of paying patients served. Consultations by numerous experts are readily available.

A wide spectrum of disorders is seen, and the patients are referred from widely dispersed areas. The cases assigned to students are carefully selected from many points of view. An effort is made to delegate as much responsibility as the trainees are capable of handling.

With all of the systematized teaching and research and the utilization of "assembly lines" of specialists, it is very important that sufficient time be spent with individual trainees, dealing not only with their immediate scientific instruction but also with their present working conditions, philosophies, future goals, etc. Appropriate stimulation and orientation toward the best objectives often promote more ultimate progress than an eloquent dissertation on medical facts. Both are important.

REFERENCES

1. Williams, R. H.: Future training in medicine and medical specialties. J.A.M.A. 167:192-199, 1958.
2. ——: Departments of medicine in 1970. I. Staff policies. Ann. Int. Med. 50:1252-1276, 1959.
3. Gregg, A.: Medical institutes. Canad. M. A. J. 70: 449-453, 1954.
4. Williams, R. H.: Departments of medicine in 1970. II. Teaching policies. Ann. Int. Med. 51:110-128, 1959.

CLINICOPATHOLOGIC CONFERENCE

Report From Veterans Administration Hospital, Hines, Illinois

Edited by William J. Donnelly, M.D., Chief, Section of Hematology

Case Report

ONE week before entering Hines Veterans Administration Hospital, a 27 year old laborer was admitted to a private hospital complaining of weakness, night sweats and a fever of two weeks' duration. Other symptoms included moderate abdominal distention and a 5 lb. weight loss. A biopsy of an inguinal node on the left side was performed. The patient was given streptomycin, tetracycline and 1 unit of blood. His condition improved slightly, and he was referred to Hines for further treatment. The past history and systemic review were noncontributory.

When he was admitted to Hines on December 23, 1958, the patient appeared to be chronically ill, but he was fairly well nourished. On physical examination, his temperature was 100.6° F., and his pulse was 108 and regular. Blood pressure was 110/62. Eyes, ears, nose, throat, heart and lungs were normal. The abdomen was distended, but it was not thought that ascites was present. The liver was felt 10.0 cm. below the right costal margin, and was smooth, firm and nontender. The spleen could be felt 15.0 cm. below the left costal margin and was similarly firm and nontender. Generalized lymphadenopathy was present. Multiple bilateral 0.5 to 1.0 cm. cervical nodes and 2.0 cm. axillary nodes were present. There also were several 1.0 cm. nodes in the right groin and large clusters of nodes up to 8.0 cm. in diameter in the inguinal and femoral regions on the left side. These nodes were relatively firm, discrete and nontender. No other abnormalities were observed.

Laboratory data—Results of urinalysis and serologic studies were negative. Levels of nonprotein nitrogen, creatinine, fasting blood sugar, cholesterol and esters were normal, and an electrocardiogram revealed no abnormalities. A chest x-ray showed no abnormal findings except for elevation of the left hemidiaphragm. Bilirubin was 0.5 mg., and thymol turbidity was 11 units. Cephalin-cholesterol flocculation was 4 plus in 48 hours. Total protein was 6.0 gm., with 3.3 gm. albumin. Psoas shadows were faintly visualized on intravenous pyelography, and the left renal shadow was displaced inferiorly. The dye appeared promptly and was excreted normally, although the lower half of the left ureter was slightly displaced medially.

The hemoglobin level was 11.4 gm., and the hematocrit reading was 34 per cent. The white blood cell count was 3400, with 65 per cent neutrophils and 34 per cent lymphocytes.

Examination of the peripheral blood film revealed moderate anisocytosis and occasional polychromatophilia, macrocytosis and target cells. Granulopoiesis was moderately toxic, and platelets appeared adequate. Aspirate from the sternal marrow was moderately hypercellular, and there was a slight increase of megakaryocytes, some of which were immature. The ratio of nucleated red blood cells to white blood cells was approximately 1:2, and the plasma cells, eosinophils, mature and immature lymphocytes, histiocytes, and reticular cells were slightly increased. Results of the Coombs test were negative.

A study of the sections of the inguinal lymph node biopsy, performed previously, revealed almost complete obliteration of the follicular architecture due to the presence of many more or less immature lymphocytes and many large, loosely grouped histiocytes. Several Reed-Sternberg giant cells, scattered plasma cells, eosinophils and mitotic figures were seen. The lymph node capsule was infiltrated by lymphoid cells in a few places.

Hospital course—The patient was initially treated with bed rest, regular diet and aspirin. During the first three weeks of hospitalization, his temperature rose to 100 or 101° F. daily. From January 10 to 13, 1959, he was given divided doses of nitrogen mustard (0.4 mg. per kilogram of body weight). His temperature promptly became normal and he improved subjectively; however, the liver, spleen and lymph nodes remained unchanged.

During the sixth week of hospitalization, the patient had fever, night sweats, weakness and exertional dyspnea. During the seventh week, his temperature spiked to 102 and 104° F., and he appeared pale and chronically ill. Generalized lymphadenopathy, including bilateral 3.0 cm. axillary nodes and 5.0 cm. inguinal and 6.0 cm. femoral clusters of nodes on the left side, was present. A 5.0 cm. mass on the left side of the pelvis was palpated. The hemoglobin level fell to 9.2 gm., and the white blood cell count was 2,850 with 76 per cent neutrophils.

On February 10, 500 cc. of blood was given and another course of nitrogen mustard (0.4 mg. per kilogram of body weight) was started. Following this treatment, the patient became afebrile and improved subjectively. The hemoglobin level rose to 10.0 gm. on February 19 and 24; however, the white blood cell count fell to 1800 and 2200 on those days, respectively. The patient had persistent slight discomfort related to the mass in the lower abdominal quadrant.

On March 3, the patient's symptoms recurred. His temperature began to rise to 102 or 103° F. daily. Rhinorrhea, productive cough and scattered rhonchi were noted. Another chest x-ray and a blood culture gave negative findings. The hemoglobin level was 6.6 gm. on March 4. The white blood cell count was 750, with 15.2 per cent reticulocytes. In addition to erythromycin and tetracycline, the patient was given nitrogen mustard (0.15 mg. per kilogram of body weight) and 3000 cc. of blood during the period from March 4 to 15. After this treatment, his fever disappeared and the hemoglobin level rose to 11.3 gm. Leukopenia persisted. Antibiotics were discontinued on March 30, and symptomatic measures controlled the upper respiratory symptoms.

On April 16, the patient began having a daily low-grade fever of up to 100° F. The hemoglobin level had fallen to 7.7 gm., and six nucleated red blood cells per 100 white blood cells were noted in the peripheral blood. On April 17, 1000 cc. of whole blood was given, and the hemoglobin level rose to 9.8 gm. Despite administration of 2 units more of whole blood, on April 30 the hemoglobin level was still only 9.6 gm. Another 500 cc. of blood was given on May 4. Low-grade fever persisted until June 28, but thereafter only an occasional elevation was noted. From May 28 to July 13, the hemoglobin level rose from 8.0 to 10.1 gm. Leukopenia persisted, and from 5 to 36 nucleated red blood cells per 100 white blood cells were noted in the peripheral blood. Polychromatophilia and basophilic stippling were observed frequently, and the reticulocyte count on June 2 was 16 per cent. Platelets varied from 66,000 to 96,000. Aspiration of the sternum and the iliac crest yielded no marrow elements. At this time, normal or negative results were obtained from

the following studies: the Coombs, van den Bergh and osmotic fragility tests, quantitative urinary and fecal urobilinogen determinations, and analyses of the stool for occult blood. The radiochromium-labeled red blood cell half-life was 12.5 days (a normal period is 22 to 28 days).

The patient was started on 40 mg. prednisone daily on June 29, and on July 13 an operation was performed.

Discussion

DR. AARON M. JOSEPHSON (director, department of hematology research, Michael Reese Hospital, Chicago): Until the time that surgery was performed on this patient, the course of his illness was some seven months. On admission to Hines, he apparently had been ill for only a short time. The unit of blood and the streptomycin and tetracycline which he received at another hospital were perhaps sufficient to confuse somewhat the true picture of his illness. He also had a biopsy on an inguinal node at that same hospital. I would like to point out here that if some form of lymphomatoid disease is suspected, this is one of the worst areas in which to perform a biopsy.

I think the most significant finding at the time of this patient's admission to Hines was the presence of splenohepatomegaly. I use this term because the description of the findings seemed to indicate that the spleen was much larger than the liver. In addition, he had generally enlarged lymph nodes, especially in the inguinal and femoral regions.

Most of the results of the initial laboratory studies were normal. The patient was moderately anemic and leukopenic, and there was an approximately normal differential. I think this is significant, because in abdominal lymphomas marked involvement of the periaortic nodes is frequently associated with a peripheral lymphopenia. In this case the leukopenia probably can be blamed on splenomegaly. I do not like the term "hypersplenism"; this is the old-fashioned splenic-inhibition syndrome.

The platelet count in this patient was not mentioned until after he had been hospitalized for about five months, at which time he was severely thrombocytopenic. However, he also had received nitrogen mustard, so I do not know whether or not he was initially thrombocytopenic. Was there any indication as to the number of platelets on admission?

DR. DONNELLY: The platelets were estimated to be quantitatively normal in the peripheral blood film.

DR. JOSEPHSON: Then the patient was not, at least not severely, thrombocytopenic initially. The anemia seems to have been a normochromic-normocytic type; there was no evidence of hemorrhage. This may be part of a splenic-inhibition syndrome. In addition, there was evidence of a hemolytic process. On March 4, the hemoglobin level was 6.6 gm., a severe leukopenia, with 15.2 per cent reticulocytes. With the hemoglobin at this level, I am assuming that the red blood cell count was about 2 to 2.5 million, which gives a reticulocyte count of about 300,000, or somewhat less than half the amount of production which should be developed if the patient's marrow had been normal. This indicates a dual cause of the anemia, decreased production and increased destruction of red cells. This is a serious situation.

The marrow in this patient was described as showing an increase in plasma cells, eosinophils, histiocytes and reticular cells. Granulopoiesis was moderately toxic, and both mature and immature lymphocytes were seen. This type of marrow is consistent with any one of a number of disease states. It is sometimes described as reactive marrow. Any sort of chronic granulomatous disease, severe infection or lymphoma can produce this type of marrow. I do not think that it is at all diagnostic; it merely indicates that a severe process is occurring. From the description of the inguinal node biopsy and other significant findings, I think we must assume at this point that this patient had Hodgkin's disease.

The patient's course was marked with subjective improvement and recurrence of symptoms. He seemed to improve following each course of nitrogen mustard, which was given in an adequate dosage. In February and again in March, recurrence of symptoms was accompanied by a fall in the hemoglobin level,

which rose in response to transfusions; however, leukopenia persisted. The hemoglobin level was again very low on April 16, indicating a rather severe hemolytic process; the patient also had severe thrombocytopenia at this time, and again he was given blood transfusions. The hemoglobin level rose, but leukopenia still persisted. The patient was pouring out nucleated red blood cells into the peripheral blood, and he had marked polychromatophilia and basophilic stippling.

The erythroblastosis may signify (1) simply a response of the marrow to the hemolytic process or (2) involvement of the marrow. Nucleated red cells frequently are seen in the peripheral blood in metastatic disease of the marrow or when any severe disease process causes the marrow, because of stress or stimulation, to open up and allow these cells to pour out. The sternum and the iliac crest were aspirated, but no marrow elements were obtained. I want to emphasize one point here. It was stated that urinary and fecal urobilinogen determinations apparently gave normal results; however, these results either were in error or were obtained in tests made on another patient. With this much evidence of hemolysis, one would expect that even with quantitatively normal urinary and fecal urobilinogen the hemolytic index would be abnormal.

We do not know what kind of an operation was performed on July 13, 1959. The possibilities include a bone-marrow transplant, another lymph node biopsy, or a pleural biopsy. However, everything points to this mass in the left side of the lower pelvis, and I think that an abdominal procedure was performed. I am not sure that such a procedure was warranted. The patient might have been more desperately ill with this mass than is indicated in the protocol, but I am forced to assume that an abdominal operation was performed. What was this mass? Was it something attached to the kidney? Was it a group of nodes? Was it something entirely different? Did this patient have another tumor?

If we assume that the primary disease in this case was Hodgkin's disease, the possibilities of a secondary infection are quite good. A chronic upper respiratory infection in a hospitalized patient with a lymphoma should suggest a staphylococcal pneumonia, possibly a staphylococcal septicemia, or perhaps an abscess in the abdomen involving the kidney. Lymphomas sometimes involve one kidney or both, and occasionally produce rather large masses either attached to or in part of the kidney. In addition to this, one always should consider the increased incidence of fungous diseases in patients with lymphomas and related disorders. Neither the course nor the laboratory findings would suggest that this patient had tuberculosis complicating the Hodgkin's disease. The literature contains reports of cases of Kaposi's sarcoma, not involving the skin, which have been misdiagnosed as Hodgkin's disease or lymphosarcoma. The pathologist, slicing the same node a number of times, will find in one part evidence of Kaposi's sarcoma and in another part evidence of Hodgkin's disease. There are one or two reports of patients observed for four or five years with a diagnosis of Hodgkin's disease who were found at autopsy to have had Kaposi's sarcoma involving the reticuloendothelial system but not the skin.

This patient did have Hodgkin's disease. I think he also had either a staphylococcal abscess of the abdomen, involving the left kidney, or a tuberculous peritonitis.

DR. WILLIAM E. FREDERICK (assistant chief, radiology service): A chest x-ray made on December 24, 1958, showed an elevation of the left hemidiaphragm; otherwise, the chest was essentially normal. Elevation of either hemidiaphragm can be caused by a number of things, including a subdiaphragmatic pathologic condition such as an abscess, eventration, interruption of the phrenic nerve, or enlargement of an organ below the diaphragm.

An intravenous pyelogram on January 7, 1959, revealed that the left kidney was considerably depressed. The right kidney also was slightly displaced downward. The left kidney is usually higher than the right, but in this case it was displaced downward. This may have been due to splenomegaly.

We concluded that there was evidence of enlargement of the spleen, that the chest was

normal, and that both kidneys were depressed because of splenic enlargement.

DR. JOSEPHSON: I find it interesting that all through this man's illness there was very little radiologic evidence of any involvement of either mediastinal nodes or pulmonary infiltration. This is rather unusual in far-advanced lymphoma involving all peripheral lymph nodes and marked hepatosplenomegaly. One wonders whether or not the primary diagnosis was really correct, because this much peripheral disease without involvement of mediastinal nodes would be rather unusual.

DR. DONNELLY: The clinical problem in this patient, in addition to the systemic manifestations of fever, sweats and weight loss, was largely that of anemia. Our concern was with the mechanism of the anemia and with the measures which might alleviate the rather brisk requirements for blood transfusions.

DR. JOSEPHSON: I think it can be safely assumed that this patient had a symptomatic hemolytic anemia, as evidenced by a rapid loss of transfused cells and a decrease in the survival time of the radiochromium-labeled red cells. In addition, he was receiving nitrogen mustard and had a disease which might well involve the marrow, although marked involvement of the marrow is rare in Hodgkin's disease. Thus, red blood cell production was decreased, and at the same time red blood cell destruction was increased.

Unfortunately, very little can be done for this condition. In some instances, steroids may reduce the severity of the hemolytic process. However, when a state of no marrow and a marked decrease in platelets is reached, as in the latter phase of this patient's course, the inability of the marrow to produce makes the use of steroids futile. When steroids are used to treat thrombocytopenic purpura, the criterion for the dosage level certainly should *not* be the platelet count; it should be the bleeding time. The effect of the steroids in controlling bleeding cannot be estimated unless one measures the bleeding time. This is a crude test, but the platelet count may never change in an autoimmune type of thrombocytopenic purpura, while the patient's bleeding time has been reduced by steroids. Even though there was no laboratory evidence of an autoimmune process in this patient, I think we can assume that such was present. He received 40 mg. of prednisone per day. We prefer to start with a higher dosage. We frequently start with 80 mg. of prednisone daily and subsequently reduce the dosage after a therapeutic response.

I think Dr. Donnelly wants me to discuss the use of bone-marrow transplants in the therapy of aplastic processes or hypoplastic-marrow syndromes. In spite of the French literature and of *Life*, *Time* and *Newsweek*, I have seen no good evidence that homologous bone-marrow transplants have done any good for anyone. There is as yet no effective method for completely destroying the immunologic system of the recipient. The use of autologous marrow obtained before treatment with nitrogen mustard or x-ray is more logical, and in these instances I think we can see more beneficial effect.

DR. ROBERT LAPPE (resident, medical service): Dr. Josephson, do you think this patient might have had a splenectomy rather than one of the surgical procedures which you mentioned?

DR. JOSEPHSON: He could well have had a splenectomy. Before splenectomy is performed for a hemolytic process and thrombocytopenia, steroid therapy should be given an adequate trial. Neither the duration nor the dosage of steroid therapy in this patient represented an adequate therapeutic trial. Therefore, I doubt that he had a splenectomy, although this is a possibility.

DR. EDWARD O. WILLOUGHBY (assistant chief, medical service): Dr. Josephson, does the failure to obtain marrow by aspiration necessarily mean that the marrow is aplastic? Isn't it possible for the marrow to be too densely packed to permit aspiration?

DR. JOSEPHSON: Frequently in lymphomas, treated or untreated, marrow cannot be obtained by standard aspiration technics. Pathologists have a nasty habit of finding bone marrow even in the worst aplastic anemia in a vertebra, rib or other bone not accessible to needle aspiration. A bone-marrow biopsy would have been interesting. I think that there

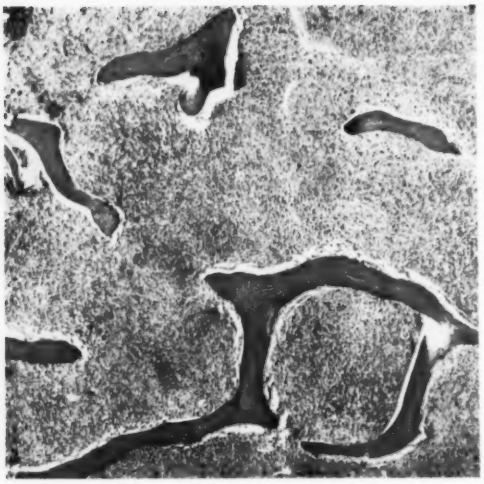


FIGURE 1. Moderate cellulosity of bone-marrow biopsy (x 30).

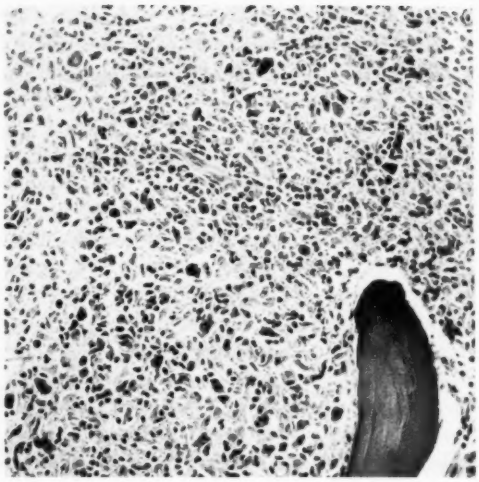


FIGURE 2. Pleomorphic infiltrate and multinuclear giant cells (x 120).

was every reason for hypoplasia to develop in this patient, considering the large amount of nitrogen mustard that he received.

DR. MYRON E. RUBNITZ (chief, laboratory service): Dr. Josephson's point about biopsy of an inguinal node is extremely important. Most adult men in the older age group have confusing inflammatory changes in their inguinal lymph nodes.

DR. WILLIAM J. GILLESBY (assistant chief, surgical service): What is the order of the desirability of biopsy in a generalized lymphadenopathy? I have found that if you biopsy inguinal nodes, strangely enough, you find that the patient has athlete's foot.

DR. JOSEPHSON: I think the important thing is to perform a biopsy on a palpable node. If you can find an enlarged node in any area other than the inguinal region, take it from that area, whether it is the axillary, epitrochlear or cervical region. If you cannot find any palpable nodes, a blind biopsy of the scalenus areas can be very helpful.

DR. RUBNITZ: The biopsy of the inguinal lymph node, which was performed elsewhere and reviewed here, showed the characteristic features of Hodgkin's disease.

The operation performed on July 13, 1959, was a biopsy of the sternum. When the bone-marrow biopsy was examined under very low magnification (figure 1), a moderate cellulosity was seen. It was immediately suspected that this marrow was composed of abnormal cells, for, although giant cells were abundant, they did not appear to be megakaryocytes. The suspicion of replacement of the marrow with abnormal cells was confirmed on higher magnification (figure 2) with the finding of a pleomorphic infiltrate composed of eosinophils, lymphocytes, abnormal histiocytes, fibroblasts and the previously described giant cells, which presented the typical appearance of Reed-Sternberg cells (figure 3). The last-mentioned cells are multinuclear giant cells with two or three nuclei, each having very distinct nuclear membranes and containing prominent eosinophilic-staining nucleoli. Some areas presented another microscopic feature of Hodgkin's disease, a fibroblastic infiltration with the proliferation of a fine, collagenic fibrillar network which progresses to frank fibrosis in later stages (figure 4).

Involvement of the bone marrow in Hodgkin's disease is very unusual and constitutes another in a long list of infiltrations in atypical areas. Because of the pleomorphic cellulosity of normal bone marrow, the finding of giant cells with characteristics of Reed-Stern-

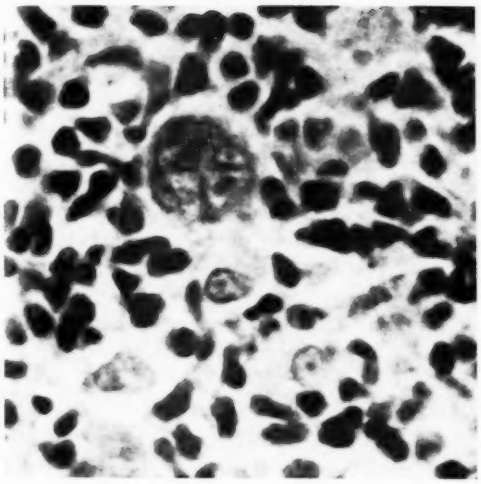


FIGURE 3. Typical multinuclear giant (Reed-Sternberg) cell (x 400).

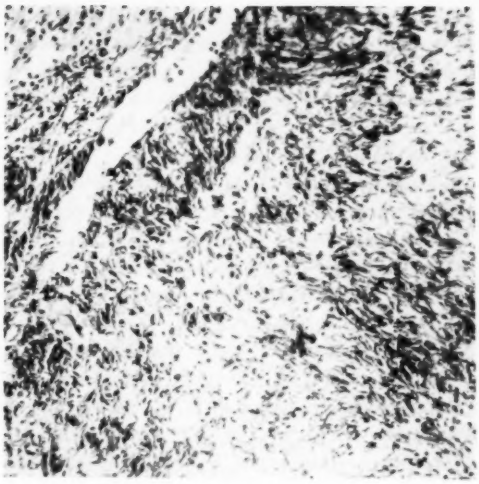


FIGURE 4. Fibroblastic proliferation and formation of fibrous tissue (x 60).

berg cells, as distinguished from megakaryocytes, is diagnostic.

DR. DONNELLY: We were strongly considering a splenectomy because of the severe hemolysis in this patient. We obtained the bone-marrow biopsy after the unsuccessful marrow aspirations in order to determine the cellulosity of the marrow before asking the surgeon to remove the spleen.

DR. ARMAND LITTMAN (chief, medical service): Are Turkel biopsies worth trying?

DR. DONNELLY: Our Turkel needle biopsies have yielded inadequate specimens. Some claim greater success with the Vim-Silverman needle.

This patient's course, following the diagnosis of Hodgkin's disease with involvement of the bone marrow, has been as follows:

To the present date (October 13, 1959), he has remained afebrile, except for having an occasional temperature rise to 100° F. His weight has remained stable. He currently is working as a full-time service man for vending machines. The lymph nodes, liver and spleen have not changed since the description last given in the protocol. The initial dosage of 40 mg. prednisone daily was given only briefly. Currently, he is receiving only 20 mg. prednisone daily. A coagulation profile obtained before the bone-marrow biopsy was normal except for a bleeding time of eight minutes and an abnormal prothrombin consumption, which presumably were caused by the quantitative decrease in the platelets. The patient did not bleed excessively at the time of biopsy.

The patient's hemoglobin level has remained between 10 and 11 gm. since the biopsy was performed, despite the persistence of reticulocytosis, erythroblastosis and thrombocytopenia. The leukopenia has persisted. Earlier this month, serum calcium, phosphorus and alkaline phosphatase were normal. It is interesting to us that the decrease in the patient's transfusion requirement cannot be attributed to the administration of steroids, since his last transfusion was given on May 4, and it was apparent at that time (before institution of steroids) that he was going into remission. Not only the systemic symptoms but also the need for transfusions subsided. During these five months he has required no transfusion and is doing well with essentially no treatment.

DR. JOSEPHSON: Dr. Donnelly brought out an extremely important point. The therapy of all malignancies of the reticuloendothelial system is more philosophic than scientific in ap-

proach. Almost all the drugs that we use are poisons; x-ray is similarly harmful. Drugs must be given with utmost caution. After a little experience in treating such individuals you frequently learn that *no* treatment is the *best* treatment. I think that more of these patients are dying today from iatrogenic diseases than from their original disease process. They come into the hospital and acquire a marrow aplasia or hypoplasia after receiving nitrogen mustard, triethylenemelamine or one of the newer oncolytic agents. While they are hospitalized, they frequently acquire an often fatal staphylococcal infection. The patient with a lymphoma should not be treated unless absolutely necessary. If you *must* treat, be willing to switch drugs if the response to the first drug is not adequate. Triethylenemelamine or some other agent might have been given to this patient instead of the third course of nitrogen mustard. The important thing is to see the patient as often as necessary and to use the drugs when necessary but *not* unless really indicated.

In almost everyone's experience, Turkel biopsies have provided notoriously poor specimens. We have used the Vim-Silverman needle with success. However, you break a needle every time, and many of the patients complain because you have to push hard to get out a piece of bone. Nevertheless, it is a good technic. In an institution such as mine, open biopsy is expensive to the patient because of operating room charges.

DR. CALVIN RADIN (staff physician, medical service): I would like to ask Dr. Donnelly what happened to the mass in the left pelvis.

DR. DONNELLY: The mass in the pelvis is still there, although it is somewhat smaller in size. It has not proved clinically troublesome.

BOOKS RECEIVED

Books received are acknowledged, and, as space permits, those of principal interest to our readers are reviewed more extensively. Reviews appear in this issue starting on page A-148; additional listings are on page A-152.

A Synopsis of Contemporary Psychiatry. By George A. Ulett, M.D., Professor of Psychiatry, Department of Psychiatry and Neurology, Washington University School of Medicine, St. Louis, and D. Wells Goodrich, M.D., Chief, Biosocial Growth Center, National Institute of Mental Health, Bethesda, Maryland. Ed. 2. 309 pages. 1960, The C. V. Mosby Company, St. Louis. $6.50.

Recent Advances in Pathology. Edited by C. V. Harrison, M.D., Professor of Morbid Anatomy, University of London Postgraduate Medical School, London, England, with 11 contributors. Ed. 7. 459 pages with 140 illustrations. 1960, Little, Brown & Company, Boston. $11.00.

The Choice of a Medical Career. Essays on the fields of medicine. Edited by Joseph Garland, M.D., Editor, *New England Journal of Medicine*, and Joseph Stokes, III, M.D., Associate in Preventive Medicine, Harvard Medical School, Boston, with 22 contributors. 231 pages. 1961, J. B. Lippincott Company, Philadelphia and Montreal. $5.00.

Quantitative Cellular Haematology. American Lecture Series. By J. M. Yoffey, M.D., Professor of Anatomy, University of Bristol Faculty of Medicine, Bristol, England. 122 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $5.50.

Current Therapy—1961. Edited by Howard F. Conn, M.D., with 12 consulting editors. 806 pages. 1961, W. B. Saunders Company, Philadelphia and London. $12.50.

Radioisotope Measurement in Nuclear Medicine. By Frank H. Low, Nuclear Division, Picker X-Ray Corporation. 67 pages, illustrated. 1960, Picker X-Ray Corporation, White Plains, New York. $2.50.

Medical Entomology. By William B. Herms, Sc.D., Late Professor of Parasitology, Emeritus, University of California, Berkeley. Revised by Maurice T. James, Ph.D., Professor of Entomology, State College of Washington, Pullman. Ed. 5. 616 pages, illustrated. 1961, The Macmillan Company, New York. $12.50.

Fetal Electrocardiography. The electrical activity of the fetal heart. American Lecture Series. By Saul David Larks, Ph.D., Assistant Professor of Biophysics, University of California School of Medicine, Los Angeles. 109 pages, illustrated. 1961, Charles C Thomas, Springfield, Illinois. $6.50.

Medical-Surgical Nursing. By Kathleen Newton Shafer, R.N., formerly Associate Professor in Out-Patient Nursing, Cornell University-New York Hospital School of Nursing, Janet R. Sawyer, R.N., Instructor, Department of Nurse Education, New York University, Audrey M. McCluskey, R.N., Associate Professor in Nursing, Cornell University-New York Hospital School of Nursing, New York, and Edna Lifgren Beck, R.N., Associate Director of Nursing Education, Muhlenberg Hospital School of Nursing, Plainfield, New Jersey. Ed. 2. 876 pages with 141 illustrations. 1961, The C. V. Mosby Company, St. Louis. $8.75.

Self-help Devices:

Homemaking: Kitchen Area Storage Facilities

EDWARD W. LOWMAN AND HOWARD A. RUSK

Institute of Physical Medicine and Rehabilitation
and the Arthritis Self-help Device Office*

New York University Medical Center, New York

THE disabled homemaker often finds it necessary to reorganize her existing storage facilities in the kitchen to accommodate limited mobility in reaching and bending. The reaching range is further decreased when the patient is urged or compelled to sit while doing many household tasks. The following suggestions are offered as aids in relocating some of the most-used kitchen equipment so that it will be within the patient's maximal reach.

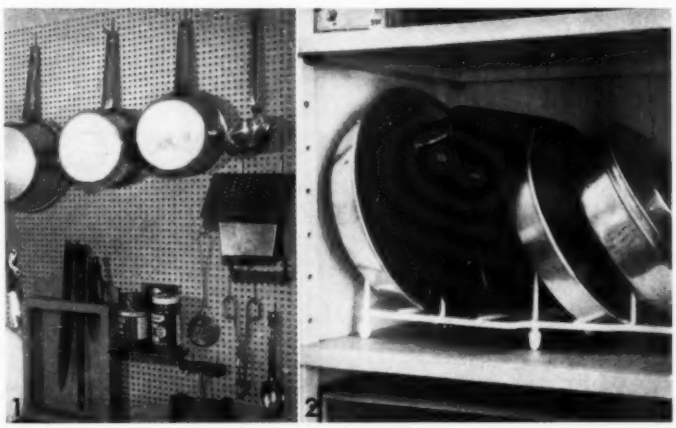


FIGURE 1. Pegboard provides a means of hanging frequently used items. Note that the knife rack permits the handles to remain upright for easy grasp.

FIGURE 2. Dish racks can be used to stack pots vertically.

*Supported at the Institute by the Arthritis and Rheumatism Foundation.

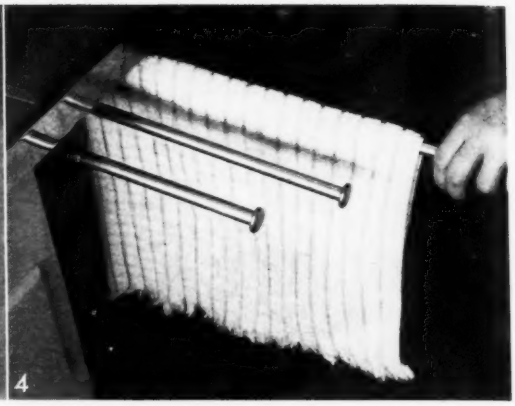


FIGURE 3. Shelf dividers utilize previously wasted space.

FIGURE 4. Sliding racks make towels and pans more easily accessible. Sliding racks for holding cups are also available.

FIGURE 5. Turntables (or Lazy Susans) bring items from the rear to the front, eliminating stretching.

FIGURE 6. Magnetized utensil holders (MAGNAGRIP®) will keep various tools ready for immediate use. Holders for cooking utensils should be located near the stove, where they are most frequently used.

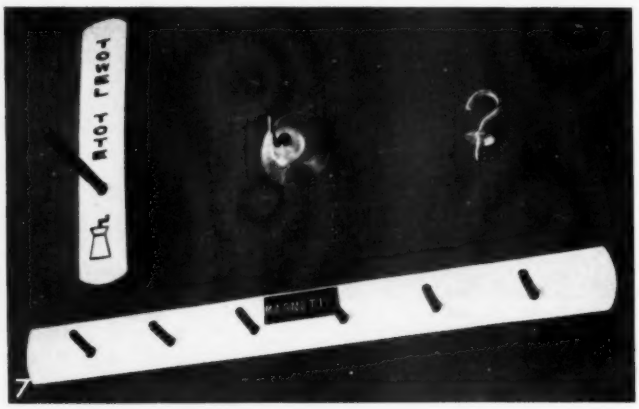


FIGURE 7. Suction hooks, screw-in hooks, magnetized Towel Totes, and Refrigopegs all provide extra hanging space within reach.

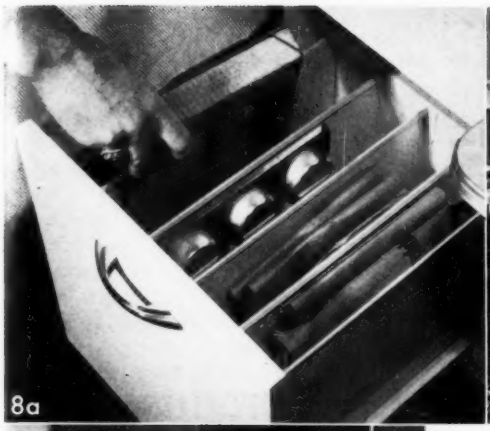


FIGURE 8. a. Vertical partitions permit upright stacking.

b and c. Revolving corner units and metal sliding drawers bring articles more readily within reach.

FIGURE 9. A reaching device should always be available to retrieve articles that have fallen to the floor and to reach articles on high shelves.

FIGURE 10. Lower narrow shelving can be improvised if space is available.

FIGURE 11. When filed vertically, utensils are accessible from a wheel chair.

Editorials

Postgraduate Medicine

Editor-in-Chief:
CHARLES W. MAYO, M.D.

Contributing Editor:
MORRIS FISHBEIN, M.D.

Executive Editor:
SYLVIA COVET

SUSPENDED JUDGMENT

THE Greek word for suspended judgment is *ankinoia.* Using this word as a title, Sir Heneage Ogilvie[1] discussed the future of general practice in Great Britain, where both general practice and specialization have changed with the coming of the National Health Service. Apparently, the National Health Service has made consultation with a specialist of their choice available to the poor, which, said Sir Heneage, "was formerly a privilege available to the rich only." He said, "It can be a cheap and easy means of keeping a querulous patient quiet for a few days longer, a device for jumping the queue of the waiting list at the hospital, or a means of giving a four guinea tip at Government expense to an impecunious consultant friend."

In Great Britain, consultation is a much more formal matter than in the United States. Thus, Sir Heneage said:

> The general practitioner is the most important person at a consultation—more important even than the patient. He alone can give the story of the illness consecutively and in true proportion. He alone can give the genetic background of the patient, and advise how his personal idiosyncrasies and his past maladies may have modified the progress of the disease. He alone of the assembled group speaks with the background and the outlook of the ordinary human being.

According to Sir Heneage, "the cult of the specialist" started in the latter half of the nineteenth century, but was latent until the end of World War I. Then experts in the use of new devices and new technics began to plan specialists' degrees and diplomas, to form specialists' associations, and to publish specialists' journals. He said, "They became closed corporations, with the self-conscious superiority of a trade union and equal power to put blacklegs out of business."

As he reviewed the current situation, Sir Heneage lamented the disintegration of medical education, a condition resulting largely from specialization.

> The specialist was first a wise and experienced doctor who devoted more and more of his time to the study of a particular method of investigation or to the treatment of certain diseases or of certain parts of the body. Then

the need for wisdom and experience was replaced by the need for special study, but the specialists still underwent a general training and the specialist departments were reference departments. Lastly came the present era, the era of specialist diplomas, specialist associations and specialist journals, the era of the closed shop in which none but those holding the right ticket are allowed access to patients of a particular type, in which the student can learn about important aspects of medicine and surgery only by attending the correct departments, in which at his Finals he is subjected to special papers and to practical examinations by specialists, in addition to those in general medicine, surgery and obstetrics. No specialist has yet advanced the thesis that the part is greater than the whole, but all of them believe in their hearts that their own part is equal to the whole.

In contrast to the disintegration of medical education, the work of the general practitioner is a continuous exercise in integration. He combines his knowledge of pathology and his observations about heredity, previous illnesses and nature of his patient, and he integrates all of this into the problem of a single human being. Sir Heneage welcomes the foundation of the College of General Practitioners, calling it "the most fortunate development in the history of British medicine." He stated:

> The most dangerous disease of the modern world is technolatry, or the worship of the expert. By the expert I mean something different from the specialist. A specialist is one who has come from the general to the particular. He has by personal study made himself master of a limited subject, and he knows where his knowledge ends and where his ignorance begins. The expert is a product of the Health Service. He has never been general. He knows a lot about something and on that ground believes that he knows all about everything. The cure for technolatry is *ankinoia.*
>
> Medicine is today overloaded and weighed down by experts. It needs above all a corps of men of wide vision to keep an eye on the experts, to interrupt their flow of eloquence with an occasional Why?, to prick the balloon of extravagant claim by the pin of recorded observation. As Huxley said many years ago, "The great tragedy of science is the slaying of a beautiful theory by an ugly fact."

Feeling that the specialist sees everything from too narrow a point of view, Sir Heneage believes that there are few expert groups whose statements and whose claims can be accepted without critical scrutiny. He said that the surgeons are prone to publish the results of a marvelous new operation before they have observed them long enough to class them as "results." The radiologists are unwilling to admit that a duodenum or a lumbar spine can be normal. He emphasized the difficulty of finding a psychiatrist who will admit that a patient is normal. Indeed, he has found that the man who enters psychiatry is often himself a psychiatric cripple who "turns to this specialty because he finds, in advising and dominating others weaker than himself, a solace and support to his shaky ego, a kingdom in which he, at any rate, is king, a course on which he can play to bogy, because he has himself defined bogy." Sir Heneage feels that the general practitioner should take the greater part of psychiatry into his own hands "because he is a normal man who is yet aware, from personal experience, of the trials, temptations and difficulties that beset others."

Next, Sir Heneage warned about statistics:

> Experts are always ready with statistics, and with a tidy explanation of everything. We must remind ourselves that life is not necessarily tidy. Because A and B have varied in the same direction to the same extent over the same period, it does not necessarily follow that B is the cause of A. Duodenal ulcer became a problem in the first 10 years of the present century, and it has become a more pressing one ever since; so has smoking of cigarettes, the consumption of canned and preserved foods, the chlorination of water, the increasing tempo of living, the use of the motor and the aeroplane, and the sale of the *Daily Mirror.* Which must be blamed?

In conclusion, Sir Heneage presented a challenge with praise to the general practitioner:

> The general practitioners of Britain will, I hope, continue to fill their time-honoured role of a body of wise men, a permanent jury, whose decision on all matters of medical advance must be final. They are the spectators on the touchline who see most of the game, because they have played it for years before the boys who have just come onto the field,

and they know that there are times when the ball should come out fast to the backs, and times when it is safer to wheel the scrum and break up with the ball at their feet. They are the men round the site watching the builders at work, men who have worked in the quarries themselves, and see where the young fellow who planned the house has gone wrong. They are the guardians of the teachings of experience and common sense. They know that the newest theory is not for that reason better than the one that preceded it, that the drug that is rare and expensive is not necessarily better than one that is common and cheap. They know that aspirin can often be substituted for cortisone, to the benefit of the purse as well as the health of the patient.

MORRIS FISHBEIN

REFERENCE

1. Ogilvie, H.: Ankinoia. Practitioner 183:737-747 (December) 1959.

LIVING ARRANGEMENTS OF THE AGED

In considering the need for federal aid to the aged, some recent statistics from the Bureau of the Census are helpful.[1] Three-fourths of the old people in the United States live in families. Almost one-fourth live alone or in households without any relative present, and only a small fraction are in nursing homes, convalescent homes or other institutions. More men than women live in families. In the group 65 to 74 years of age, 84 per cent of the men and 71 per cent of the women live in families. The higher percentage of older men living in families is believed to be due to the fact that there are fewer widowers than widows among the older age group. Moreover, widows are usually better off financially, and a recent wisecrack asserts that "the widows look better than the married women." (Perhaps they try harder.)

Many old people, as I have discovered by a personal survey, do not want to leave their homes when the spouse dies. Moreover, many of the older women are reluctant to live with their families; as one said to me, "I get no pleasure out of dishwashing and baby-sitting." According to the most recently available data, elderly widows prefer to live apart from their married children if they have the resources and are in good health. Once established, old people do not change their place of residence as often as younger people do. The rapid accumulation of the aged among us has created a need for far more study of the needs of the older people.

MORRIS FISHBEIN

REFERENCE

1. Living arrangements and mobility of the aged. Statist. Bull. Metrop. Life Insur. Co. 41:6-8 (August) 1960.

INSTITUTIONALIZED POPULATION OF MINNESOTA

In 1958, a survey of the entire institutionalized population of Minnesota was conducted under the direction of the University of Minnesota's Industrial Relations Center. The objective was primarily to determine the scope of the problem of caring for the handicapped in Minnesota. Questionnaires were mailed to each of the 641 hospitals, special institutions, schools and nursing and boarding-care homes.

Mental retardation was the most significant disability of institutionalized handicapped persons less than 14 years of age. Persons with emotional and mental disabilities made up almost three-fourths of the number of institutionalized handicapped persons in the productive labor force group aged 14 to 65 years. In people more than 65 years of age, neuropsychiatric and cardiovascular handicaps were most prevalent, being found in more than half of all institutionalized persons in this age group.

Currently, about 35,000 handicapped people are hospitalized or institutionalized in Minnesota.[1] They occupy more than 70 per cent of the beds available for the care of patients, and almost half of these patients are more than 65 years old.

MORRIS FISHBEIN

REFERENCE

1. Carroll, S. J., Jr.: The institutionalized population in Minnesota. Pub. Health Rep. 75:823-826 (September) 1960.

...leading to specific, demonstrated advantages in cholesterol-lowering therapy

particularly in patients with coronary artery disease, generalized atherosclerosis, and other conditions thought to be associated with abnormal cholesterol metabolism

MER/29 REDUCES CHOLESTEROL IN AS MANY AS 8 OUT OF 10 PATIENTS: MER/29 reduces both serum and tissue cholesterol without strict adherence to diet. Although some physicians prefer to use MER/29 in conjunction with controlled diets, cholesterol can be reduced successfully without such limitation.

CONCURRENT BENEFITS REPORTED IN SOME PATIENTS: In patients with coronary artery disease, some of the concurrent benefits reported include decreased incidence and severity of anginal attacks, improved ECG patterns, diminished nitroglycerin dependence, and increased sense of well-being.

MER/29 HAS PRODUCED FEW SIDE EFFECTS, NO TOXICITY: Patients have been treated with MER/29 for continuous periods up to 19 months. In no case has there been evidence of serious toxic effects on the function of any vital organ or system. Side effects (nausea, headache, dermatitis) are rare and have usually been associated with dosages greater than those recommended for effective therapy.

MER/29 is compatible with other cardiovascular therapies. It can be used along with measures which control anxiety, hypertension, obesity and other conditions associated with cardiovascular disorders. These include nitroglycerin, PETN, and anticoagulants.

CAUTION: Since long-term MER/29 therapy may be necessary, periodic examinations, including liver function tests, are desirable. Also, since MER/29 inhibits cholesterol biosynthesis, and cholesterol plays an important role in the development of the fetus, the drug is *contraindicated in pregnancy.*

DOSAGE: One 250 mg. capsule daily, before breakfast.

SUPPLIED: Bottles of 30 pearl gray capsules.
Complete bibliography and product information available on request.

MER/29

(triparanol)

Merrell
SINCE 1828

The Wm. S. Merrell Company
Division of Richardson-Merrell Inc.
Cincinnati, Ohio • Weston, Ontario

Trademark: MER/29®

Great Names in American Medical History

New York

Austin Flint, Sr., M.D.

This is one of a series of biographical sketches of outstanding physicians of the past from each of the 50 states. Selection of subjects has been made by the medical society of each state or its designated committee.

THE State of New York is represented in medical history by numerous distinguished physicians. The Council of the Medical Society of the State of New York approved the name of Austin Flint, Sr. as its representative among the distinguished physicians selected for this series in POSTGRADUATE MEDICINE.

Dr. Austin Flint was the son and grandson of physicians. He was born in Petersham, Massachusetts, in 1812, and graduated from Harvard Medical School in 1832. After a short period of practice in Boston he moved to Buffalo, New York, where he helped to found the Buffalo Medical College and became its professor of medicine. During his career as a teacher, he was professor of medicine at Buffalo, Chicago, Louisville, New Orleans and New York. He kept complete and detailed records of his work, which amounted to almost 17,000 pages.

Austin Flint was a voluminous writer. His books "Physical Exploration and Diagnosis of Diseases Affecting the Respiratory Organs," published in 1856, and "Compendium of Percussion and Auscultation," 1864, went through five editions. His "Manual of Percussion and Auscultation," 1876, went through eight editions. "A Practical Treatise on Diseases of the Heart" was published in 1859, and "A Treatise on the Principles and Practice of Medicine," published in 1866, became a classic. The complete list of his writings contains 200 articles and six books.

Dr. Flint was particularly a student of physical diagnosis. Having studied under James Jackson, he was an enthusiastic admirer of Laennec. Flint championed the methods of auscultation. He is said to have introduced the terms "cavernous respiration" and "bronchovesicular respiration," and among medical diagnostic signs Flint's murmur is widely recognized as an apical diastolic murmur sometimes heard in aortic regurgitation. Dr. Ralph Major has said of him, "No man had a greater influence in his time on American medicine." Dr. Flint died in 1886.

when allergy looms large in the life of your patient...

relieves the symptoms of food allergy When the allergic patient can't resist eating an offending food, the ensuing punishment is often out of all proportion to the nature of the "crime." In such cases, BENADRYL provides a twofold therapeutic approach to the management of distressing symptoms.

antihistaminic action A potent histamine antagonist, BENADRYL breaks the cycle of allergic response, thereby relieving gastrointestinal upset, urticaria, edema, pruritus, and coryza.

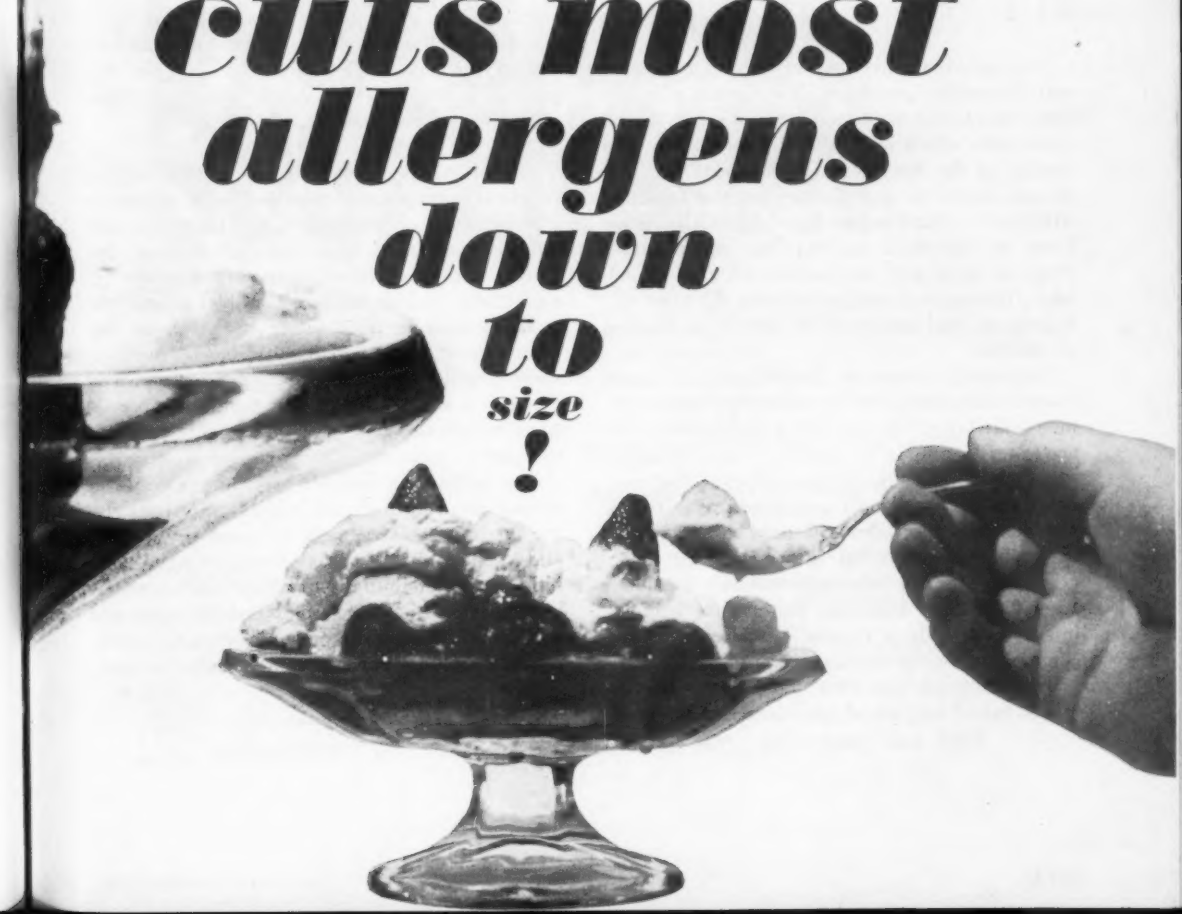
antispasmodic action Because of its inherent atropine-like properties, BENADRYL affords concurrent relief of gastrointestinal spasm, abdominal pain, nausea, and vomiting.

PARKE-DAVIS
PARKE, DAVIS & COMPANY, Detroit 32, Michigan

BENADRYL®

antihistaminic-antispasmodic

cuts most allergens down to size!



THE MEDICAL *Bookman*

► INFECTIOUS DISEASES OF CHILDREN

By Saul Krugman, M.D., Professor and Chairman, Department of Pediatrics, New York University School of Medicine, New York, and Robert Ward, M.D., Professor and Head, Department of Pediatrics, University of Southern California School of Medicine, Los Angeles. Ed. 2. 398 pages with 55 illustrations and seven color plates. 1960, The C. V. Mosby Company, St. Louis. $13.00.

The authors of this book have set a dangerous and demanding precedent. Two years after the first edition was published, they have produced a successor which is justified by the amount and quality of the new material included. The ambitious assault on viral diseases that was launched with tissue culture technics and received impetus from the successful poliomyelitis immunization program is largely responsible for this knowledge. This second edition includes the most significant clinical aspects of the infectious diseases of children.

The useful chapter on the diagnosis of acute exanthematous diseases is prefaced by some common-sense warnings concerning the necessity for accurate diagnosis of rashes. This discussion graphically relates the serious sequelae that may befall the patient, family and community from a misdiagnosed rash. Several new chapters have been added, and recent information on many other subjects has been appropriately included. In spite of these additions, the authors' original intent to provide a concise description of the common infectious diseases is preserved.

The admirable but often monotonous brevity is punctuated by clinical aphorisms that the reader will recognize as the hallmark of the physician who has spent his share of hours at the bedside. While there may be minor caviling about the appropriateness of some of the charts, this should not disturb the host of practitioners who will find the book a useful and practical companion.

J. C. D.

► PROCEDURES IN VASCULAR SURGERY

By Richard Warren, M.D., Clinical Professor of Surgery, Harvard Medical School, Boston. 211 pages, illustrated. 1960, Little, Brown & Company, Boston and Toronto. $12.00.

Combining diagrammatic illustrations and a practical commentary, this book will appeal to a wide range of physicians. For those not specifically concerned with vascular surgery, the simple and clear illustrations will provide insight into certain technical problems and the methods used in their solution. For those surgeons faced with vascular problems in their daily practice, the practical, experience-proved comments, along with the illustrations of variations in technic, may contribute significantly to the care of their patients.

The author has been realistic in presenting a section on amputations, which, unfortunately, are an important segment of vascular surgery. His emphasis on the vascular surgeon's responsibility in the rehabilitation of these patients seems appropriate. The range of procedures presented will be of interest to general surgeons whose practice includes considerable vascular surgery.

P. E. B.

(Continued on page A-151)

- **BROAD-SPECTRUM BACTERICIDAL ACTION**
- **ANTI-INFLAMMATORY ACTION**
- **RARELY SENSITIZES**

Topical hydrocortisone provides symptomatic relief of edema, pain and photophobia, and curbs neovascularization, while polymyxin B and neomycin eradicate most pathogens invading the eye, including Pseudomonas.

'CORTISPORIN'® brand OPHTHALMIC SUSPENSION

Each cc. contains:

'Aerosporin'® brand Polymyxin B Sulfate	10,000 Units
Neomycin Sulfate	5 mg.
Hydrocortisone (1%)	10 mg.

Indicated in bacterial, allergic, vernal and phlyctenular conjunctivitis; blepharitis; episcleritis; iritis; anterior uveitis; interstitial, sclerosing, postoperative or acne rosacea keratitis; chemical and thermal burns of the cornea.

Application: Apply 1 or 2 drops in the affected eye every 3 or 4 hours, depending upon the severity of the condition. In acute conditions, the drops may be used at more frequent intervals, if required.

Caution: Not recommended for herpes corneae (dendritic corneal ulcers) or conditions involving the posterior segment of the eye.

Available in bottles of 5 cc. with sterile dropper.

BURROUGHS WELLCOME & CO. (U. S. A.) INC., Tuckahoe, New York

metabolic therapy in the "therapeutic" jar

All alcoholics, whether cirrhotic or not, should receive high levels of B-complex and C vitamins[1] as provided by STRESSCAPS, since the reversal of nutritional failure and its resultant morbidity depends largely on the water-soluble vitamins. Therapeutically important, the decorative jar serves as a constant dosage reminder for the alcoholic patient... who frequently is antagonistic to rehabilitation.

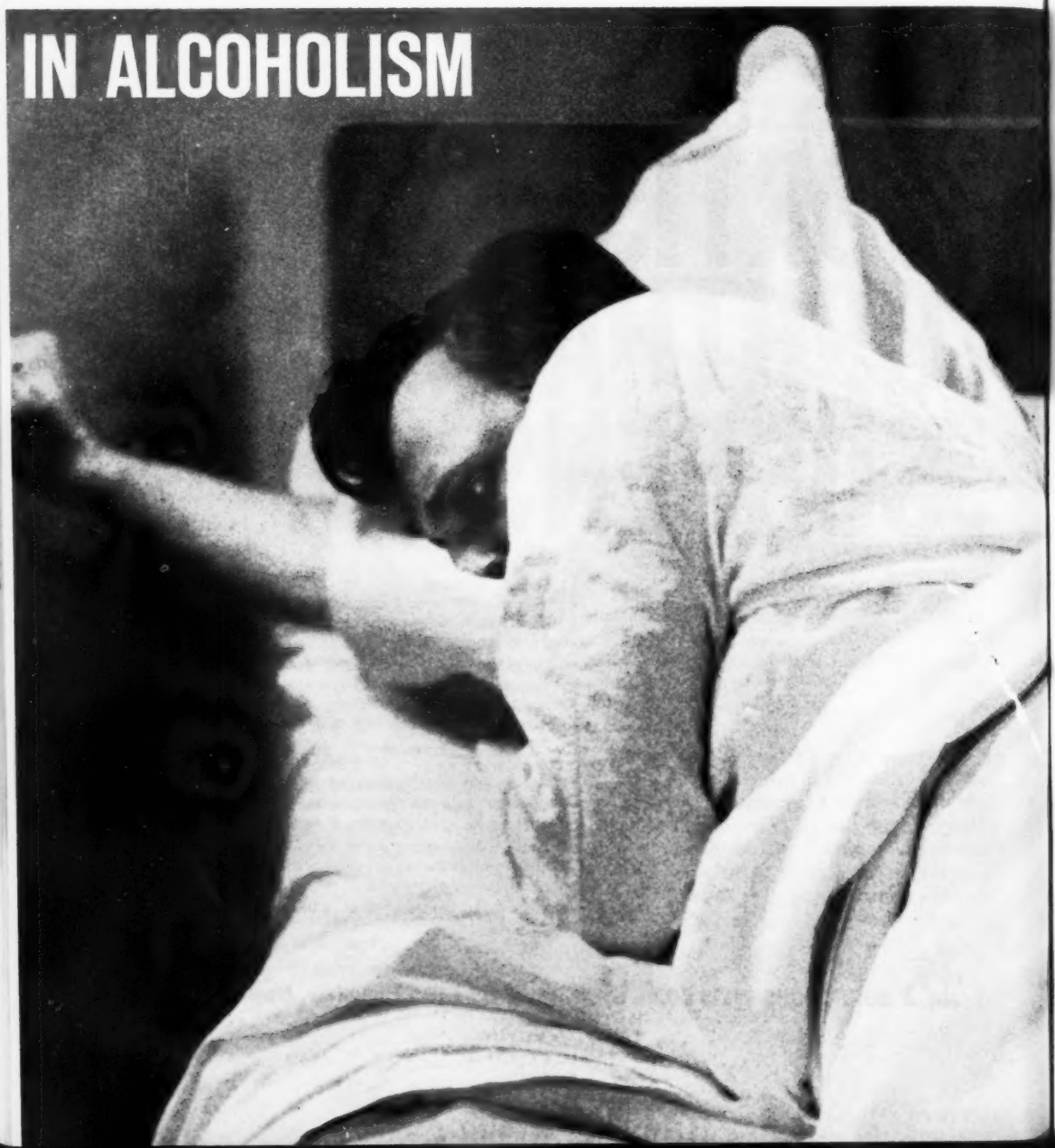
Each capsule contains: Thiamine Mononitrate (B_1) 10 mg., Riboflavin (B_2) 10 mg., Niacinamide 100 mg., Ascorbic Acid (C) 300 mg., Pyridoxine HCl (B_6) 2 mg., Vitamin B_{12} 4 mcgm., Calcium Pantothenate 20 mg., Vitamin K (Menadione) 2 mg. Average dose: 1-2 capsules daily.

1. Davidson, C. S.: Am. J. Med. 25:690 (Nov.) 1958.

LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

STRESSCAPS

Stress Formula Vitamins Lederle



► HEALTHY BABIES—HAPPY PARENTS

By Henry K. Silver, M.D., Professor of Pediatrics, C. Henry Kempe, M.D., Professor and Chairman, Department of Pediatrics, University of Colorado School of Medicine, and Ruth Svibergson Kempe, M.D., Denver. 228 pages, illustrated. 1960, The Blakiston Division, McGraw-Hill Book Company, Inc., New York, Toronto and London. $4.50.

Written in simple language that can be understood by the layman, this book is an up-to-date source of information concerning the problems of rearing infants and children that beset all new parents. The authors are nationally recognized pediatricians whose experience is wide and whose advice is authoritative.

The material is presented in a catechetic style reminiscent of a similar volume by L. Emmett Holt, Sr., "The Care and Feeding of Children," which was in vogue among an earlier generation. The questions are those frequently asked of persons responsible for the care of infants and children. Information pertaining to the monthly development of the child up to the age of one year is given in the first part of the book, while the second part is concerned with training problems and with the general management of children. Excellent illustrations and line drawings amplify the text.

S. D. M.

► SURGICAL DISEASES OF THE PANCREAS

By John M. Howard, M.D., Professor and Chairman, Department of Surgery, Hahnemann Medical College and Hospital, Philadelphia, and George L. Jordan, Jr., M.D., Associate Professor of Surgery, Baylor University College of Medicine, Houston, with nine contributors. 607 pages with 197 illustrations. 1960, J. B. Lippincott Company, Philadelphia and Montreal. $20.00.

The surgical aspects of diseases of the pancreas are more than adequately covered in this volume. The authors have brought together into one work all the current knowledge about pancreatic diseases, particularly those of special interest to the surgeon.

Exhaustive study and coverage of the current literature also have been accomplished, and each chapter is a treatise on some aspect of pancreatic disease. The medical treatment and the surgical management of diseases of the pancreas have been equally well covered. Whenever possible, the authors explain the treatment used on the basis of the existing pancreatic physiologic status. All sections are well illustrated with drawings, roentgenograms and photographs.

W. H. R.

► DERMATOLOGY
Diagnosis and Treatment

By Marion B. Sulzberger, M.D., Professor and Chairman, Department of Dermatology and Syphilology, New York University School of Medicine and New York University Post-Graduate Medical School, Jack Wolf, M.D., Attending Dermatologist, Grand Central Hospital, and Victor H. Witten, M.D., Associate Clinical Professor of Dermatology and Syphilology, New York University Post-Graduate Medical School, with the collaboration of Alfred W. Kopf, M.D., Assistant Clinical Professor of Dermatology and Syphilology, New York University Post-Graduate Medical School, New York. Ed. 2. 615 pages, illustrated. 1961, The Year Book Publishers, Inc., Chicago. $14.00.

Many monographs on dermatology have been published during the past three or four years, and each has its place. This volume is an excellent short treatise on the subject. The pictures are very good, and interesting aspects of dermatology are discussed. Emphasis is placed on certain vital subjects, including the principles of topically applied medications, application of carbon dioxide snow under physical agents, antibiotics, and corticosteroids.

Like many writers, the authors continually discuss the spontaneous evolution of birthmarks in from five to seven years. I cannot understand why anyone wants to wait this long when very small amounts of radiation therapy, preferably from radium, will stimulate birthmarks to undergo change. Administration of less than 400 gamma roentgen units will start a cavernous hemangioma toward spontaneous recovery, and the child is free of the tumor by the time he is old enough to remember. There is very little total-body radiation in this type of radium therapy, and it is not harmful.

J. H. L.

(Continued on page A-152)

Two complementing books which can help you solve all your obstetric problems!

Just Published! Willson

ATLAS OF OBSTETRIC TECHNIC

This new Mosby atlas, authoritatively written by an eminent obstetrician, J. Robert Willson, M.D., is a practical guidebook containing 120 large, individual step-by-step drawings which clearly illustrate every step in every type of normal delivery. It can assist you in the management of complications which may arise during late pregnancy or labor. You'll find it is masterfully illustrated with original drawings by Miss Daisy Stilwell.

Dr. Willson's new book is available in two editions: the deluxe edition for the physician who realizes that this book is a lifetime investment and as such, should be printed on one of the finest paper stocks obtainable and encased in an elegant binding; and the standard edition produced on the same quality stock and with the same substantial binding found on many other important Mosby reference books. The content in both editions is identical.

By J. ROBERT WILLSON, M.D., M.S., Professor of Obstetrics and Gynecology, Temple University School of Medicine, Philadelphia, Pa.; With original illustrations by DAISY STILWELL. Just published. 304 pages, 8½" x 11", 56 full page plates. Deluxe edition, $14.50. Standard edition, $12.50.

Just Published! New 6th Edition Willson

MANAGEMENT OF OBSTETRIC DIFFICULTIES

The new 6th edition of this well liked clinician's guidebook gives the physician who practices obstetrics a practical and direct approach to diagnosis and treatment of normal and abnormal pregnancy and delivery. More importantly, it is a practical guide to thoroughly tested procedures for the management of obstetric difficulties and emergencies. Operative techniques are described and effectively illustrated. Much of the book is rewritten to incorporate recent changes in diagnostic methods and therapeutics.

Revised by J. ROBERT WILLSON, M.D., M.S. Ready in April. 6th edition, approx. 735 pages, 6¾" x 9¾", 323 illustrations, 1 color plate. About $16.00.

Order on 30 Day Approval!

THE C. V. MOSBY COMPANY
3207 Washington Blvd., St. Louis 3, Mo.

I accept your offer to examine a copy of the book(s) checked below on 30 day approval without charge or obligation. A remittance with this order will save the mailing charge.

Willson, ATLAS OF OBSTETRIC TECHNIC
☐ **I prefer the deluxe edition, priced at $14.50**
☐ **I prefer the standard edition, priced at $12.50**
☐ **Willson, MANAGEMENT OF OBSTETRIC DIFFICULTIES**
☐ **Payment enclosed (Same return privilege)** ☐ **Charge my account** ☐ **Open a new account for me**

_____, **M.D.**
Address _____
City _____ **Zone** _____ **State** _____
This offer is limited to the continental U. S. only. **PM-4-61**

► INSTRUCTIONAL COURSE LECTURES

Edited by Fred C. Reynolds, M.D., St. Louis. American Academy of Orthopaedic Surgeons. Vol. 17. 421 pages, illustrated. 1960, The C. V. Mosby Company, St. Louis. $18.50.

The seventeenth volume of the instructional course lectures given at the annual meeting of the American Academy of Orthopaedic Surgeons is as attractive and informative as its predecessors have been. The material covered includes fractures, bone graft surgery, orthopedic treatment for children, and athletic injuries. The matching of the illustrations with the text is notable. As in previous volumes, noted authorities are represented. Every effort has been made to bring the material up to date and to allow expression of divergent opinions where justifiable.

For the orthopedic resident, the orthopedist or any interested physician, this volume will be a worthwhile acquisition.

E. W. J.

Books received are acknowledged in this department. As space permits, books of principal interest to our readers will be reviewed more extensively. Additional listings will be found on page 430 of this issue.

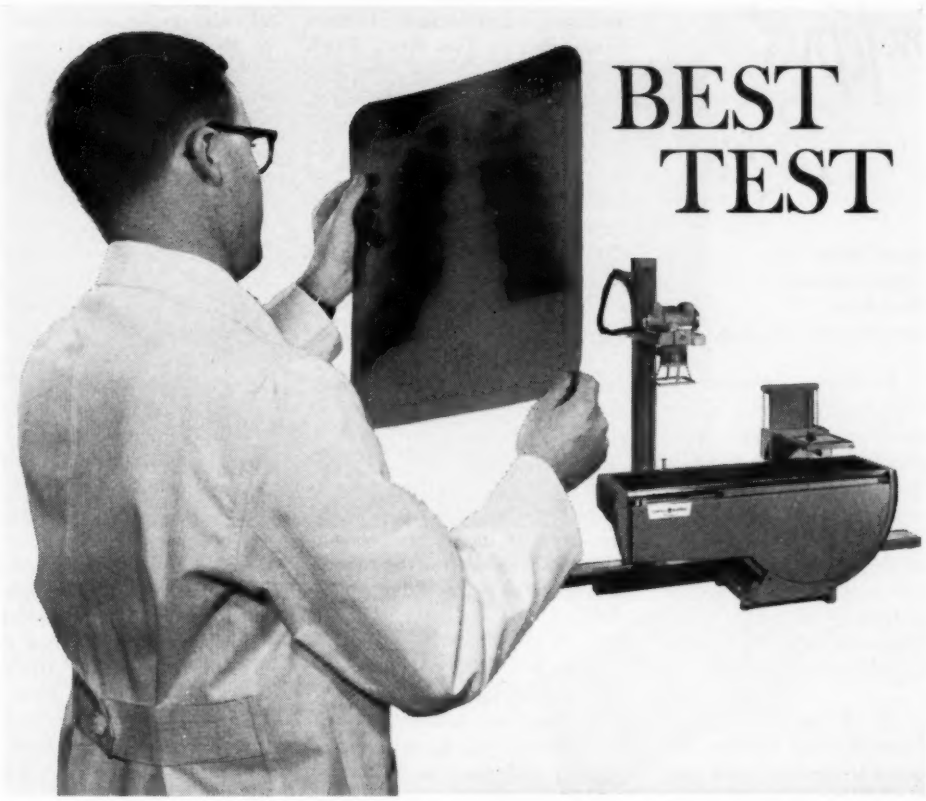
Henry Stanley Plummer; a Diversified Genius. By Fredrick A. Willius, M.D., formerly Head, Section on Cardiology, Mayo Clinic, Rochester, Minnesota. 71 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $4.50.

Culture Methods for Invertebrate Animals. Edited by Paul S. Galtsoff, U. S. Bureau of Fisheries, Frank E. Lutz, Paul S. Welch and James G. Needham, Cornell University, Ithaca, New York. 590 pages, illustrated. 1950, Dover Publications, Inc., New York. $2.75.

The Hand; a Manual and Atlas for the General Surgeon. By Henry C. Marble, M.D., Consulting Surgeon to the Massachusetts General Hospital, Boston. 207 pages with 58 plates. 1961, W. B. Saunders Company, Philadelphia and London. $7.00.

Good English for Medical Writers. By Ffrangcon Roberts, M.D. 179 pages. 1960, Charles C Thomas, Springfield, Illinois. $4.50.

Antisera, Toxoids, Vaccines and Tuberculins in Prophylaxis and Treatment. By H. J. Parish, M.D., Clinical Research Director, Wellcome Foundation Ltd., and D. A. Cannon, M.B., Medical Advisor, Wellcome Research Laboratories, Beckenham, England. Ed. 5. 288 pages, illustrated. 1961, E. & S. Livingstone Ltd., Edinburgh and London. Distributed by The Williams & Wilkins Company, Baltimore. $8.50.



BEST TEST

...the proof of the Patrician "200" is in the radiograph!

When you choose x-ray for private practice, look at performance as well as the price tag. "Economy" that is gained by short-cuts in table design or a reduction in power may mean slow exposures, blurred radiographs and repeated retakes. General Electric's Patrician "200" combination is designed with adequate power for private practice — a full 200 ma to stop anatomical movement sharply and clearly. Many other features found in larger installations are engineered into the Patrician: 81″ table, independent tubestand, shutter limiting and automatic tube protection, to name just a few. And, considering its *uncompromising* G-E quality, this Patrician "package" is remarkably low priced.

Rent the Patrician through the G-E Maxiservice® plan that provides the complete installation, *including* maintenance, parts, tubes, insurance, local taxes — *everything* in one monthly fee. Get details from your G-E x-ray representative or mail coupon.

Progress Is Our Most Important Product

GENERAL ELECTRIC

General Electric X-Ray Department
Milwaukee 1, Wisconsin, Room D-41

Send me: ☐ Patrician bulletin
☐ Maxiservice bulletin

Name_____

Address_____

_____

DR. Pepys' Pages

Personal Diary
and Observations on
Medical Life
by MORRIS FISHBEIN, M.D.

Feb. 1—Mistress Pepys concludes her drive for the March of Dimes, equaling last year's total. Reading "Laennec, His Life and Times," by Dr. Roger Kerbran—quite certainly superior to any of many biographies heretofore published. The staid *New York Times*, noting that burglars stole 500 girdles from the Warner Company, anticipates that they will get a long stretch.

Feb. 2—From New York came Peter Warren, Gordon and Bernheimer to develop some new platters of "The Voice of Medicine" for the Borden Company. In the evening with the Kirsners, Friedells and Joel Goldblatts to the Tavern Club for a good dinner, and chatted with Judge LaBuy and his lady. Then to the opening of the American Ballet for a magnificent performance, especially by Maria Tallchief, of "Miss Julie."

Feb. 3—At noon to the American Hospital Association, which has a marvelous new building in Chicago; met there the librarian, Mrs. Helen Yast, and viewed with her the beautiful apartments for the executives and the meeting halls and cafeteria. Then to speak on the scope of medical publications. There also spoke the Misses Dunlap and Lambertsen, and many questions came from the audience, which included Colonel Frank Rogers, Tom Keys, Ralph T. Esterquest of the Harvard Medical Library, and many others in related medical librarianship. A vast snow and cold descended on Chicago, and old Pepys departed home and read a little of Theodor Reik's work on "Sex in Man and Woman: Its Emotional Variations," which he discusses fluently with many anecdotes.

Feb. 4—To the ballet, where were dances especially for the children, including such bits as "Peter and the Wolf" and "Graduation Ball," and the audience seemed to be about two-thirds small fry. In the evening to dine with the Friedells for the twenty-first birthday of the eldest grandchild.

Feb. 5—All day in bed with what the diagnosticians used to call "intestinal influenza," and such misery as to make even reading difficult.

Feb. 6—At noon came our new health commissioner, Dr. Samuel Andelman, and his assistant, my old classmate Edward Buckman, to confer on new technics in health education. Then all of us to a luncheon which Mistress Pepys arranged for the ladies who will aid her in the campaign for funds for the Chicago Heart Association. Here also were Louis DeBoer and Burton Grossman of La Rabida, along with Georgianna Richards and many distinguished ladies.

Feb. 7—Early to my physician, Charles Lawrence, who gave me my regular checkup; it would seem that I am as good as if not even better than a year ago. Thereafter also for x-rays to Baker and Sammet, who found all clear on the inside front. Next to the Chicago Heart Association to preside at the meeting of the Public Health Education Committee, where were also Foa, Lepper, Willis Potts, Louis DeBoer, Barbara Friedell, Mr. McMaster of the Museum of Science and Industry, Butler Laughlin of the Chicago schools, Professor McEldowney, Mrs. Sparmacher, and others of the staff, including Frances Karlsteen, Bea Fox, Joel Edelman and Mary Courtenay.

Next to entertain Mr. Just of *Newsweek*, who would have information on the care of the aged. In the evening dined with the Albert Fishbeins.

Feb. 8—By early plane to Toronto for a layover and lunch and then on to Ottawa, where A. Hurtig came to meet the airplane. With him to view the great growth in Ottawa since old Pepys visited the Canadian capital. Then to the Chateau Laurier to meet with the press. Next to the Hunt Club, where the Academy of Medicine held its annual dinner at which Hurtig, the president, presided. A citation was presented to the psychiatrist Cathcart for his years of service, and he reminisced delightfully of the war. Then Tour introduced old Pepys, who spoke of current crises, after which Dr. Maloney gave kind remarks.

Feb. 9—Again on the plane over the same route. All afternoon busy at the desk and in the evening to hear the Chicago Symphony Orchestra with Hendl directing and Milstein playing.

Feb. 10—Early to my dentist for the annual repairs before starting abroad. Then back at the desk for a day of toil, and in the evening at "Scrabble," losing three times to Mistress Pepys.

(Continued on page A-164)

Check YOUR preference of

BARD-PARKER STERILE BLADES

in the puncture-resistant *easily* opened package

It's Sharp

CARBON

SHARP at equal hardness—carbon holds its cutting edge longer.

RIGID the 'RIB'—exclusive with the B-P RIB-BACK carbon steel blade gives extra rigidity. Rolling a 'rib' on stainless is difficult and too costly.

SAFE danger of breakage during surgery is minimized—carbon has a greater degree of toughness without embrittlement.

STAINLESS

CORROSION RESISTANT will not corrode when subjected to a reasonable period of thermal sterilization.

ECONOMICAL resterilization of exposed but unused blades eliminates 'discards'—saves costs.

TIME-SAVING may be attached to handles for emergency use in put-ups involving cardiac arrest, tracheotomy, paracentesis, or wherever pre-assembly is necessary.

BARD-PARKER BLADES are available:

Sterile B-P RIB-BACK carbon steel (individual package)
B-P stainless steel (individual package)

Non-Sterile B-P RIB-BACK carbon steel (6 of one size per package)
B-P RACK-PACK RIB-BACK carbon steel (gross and half gross units of one size)

B-P **BARD-PARKER COMPANY, INC.**
DANBURY, CONNECTICUT
A DIVISION OF BECTON, DICKINSON AND COMPANY

BARD-PARKER • B-P • RIB-BACK • RACK-PACK • IT'S SHARP are trademarks

Feb. 13—At noon to a luncheon for the Jackson Park Hospital Auxiliary, where well-nigh 200 ladies came full of grace, beauty and enthusiasm. Mistress Pepys presided, and speeches were made by Drs. Friedell, Gertz and Fishbein, and also by the administrator Ellis and Mistress Friedell. Mademoiselle Bickas of the Lyric Opera sang delightfully. Next to consult with Dr. Lawrence, and all the findings were satisfactory. So the Friedells came to dinner and to say Godspeed for our journey.

Feb. 14—Early awake and to the airport for New York, meeting Barksdale Penick on the plane and discussing with him the Food and Drug Administration. To the Waldorf, where were Kahoe, Bill White, Silver and Sammis for discussions. Afterward came Brainin of the Weizmann Institute and then Frances Holtzman with Dr. Revici, who will print a book of his work. Next came Stan Henwood and Vi and Peter Warren, and with them to the Waldorfkeller. And all the friends were on the telephone with their farewells.

Feb. 15—To London in six hours, where the pilot took a look at the ground and changed his mind, so we went back to Shannon and sat in the airport looking at Irish goods until midnight. Then by bus to Limerick, being deposited at 1:30 A.M. in the Royal Cruise Hotel, founded in 1791 and not much changed since. En route read "Peaceable Lane," by Keith Wheeler, which makes the problems of integration in housing graphic indeed.

Feb. 16—Back to the airport. On the 10 o'clock plane to London and, after scurrying from one airline to another, on a Sabena to Brussels, as all the continent was shrouded in fog. Then from Brussels in a hired car with a driver to Amsterdam in four hours in a fog with 10 ft. of visibility, arriving at the Amstel Hotel at 8 P.M. Here came the Cauveriens with Dr. Boudijk Bastiaanse to dine, and later the Van Tongerens.

TWO SHAGGY DOG TALES

A gorilla came into a bar, ordered a Scotch and soda and proffered a $20 bill. The bartender showed it to the owner, who said, "This is just a stupid ape; give him five dollars change." The bartender complied, and when the gorilla did not remonstrate, said, "We don't get many gorillas here as customers." The gorilla answered, "At the price you charge for Scotch, I'm not surprised at all!"

* * *

A man at a bar ordered a Martini. A monkey, playing around the bar, whisked its tail into the drink. The customer complained, but the bartender disclaimed any responsibility, saying that the monkey belonged to the piano player. The customer walked over to the piano and said, "Do you know the monkey got his tail in my Martini?" "No," answered the piano player, "but if you can hum a few bars I might be able to follow you."

* * *

Feb. 17—To *Excerpta Medica* for a full day of conferences with Van Tongeren, Cauverien, Dr. DeVaal and Polak. In the evening with the Van Tongerens and Dr. and Mrs. Van Bausekom for dinner at Adrian's.

Feb. 18—This day *Excerpta Medica*'s chief editorial board—Professors Woerdeman, Ogilvie and Fishbein—in session with the staff designing new projects and improvements. At night to dine with the ladies at Dikker and Thijs'.

Feb. 19—By KLM to Paris, again arriving in fog. To the Ritz, and then walked the Champs Élysées to the American drugstore near the Arch of Triumph.

Feb. 20—Pleasant sunshine in Paris, and wandered among the shops with Mistress Pepys. In the evening dining in the Ritz and then to see a vaudeville show climaxed by Edith Piaf.

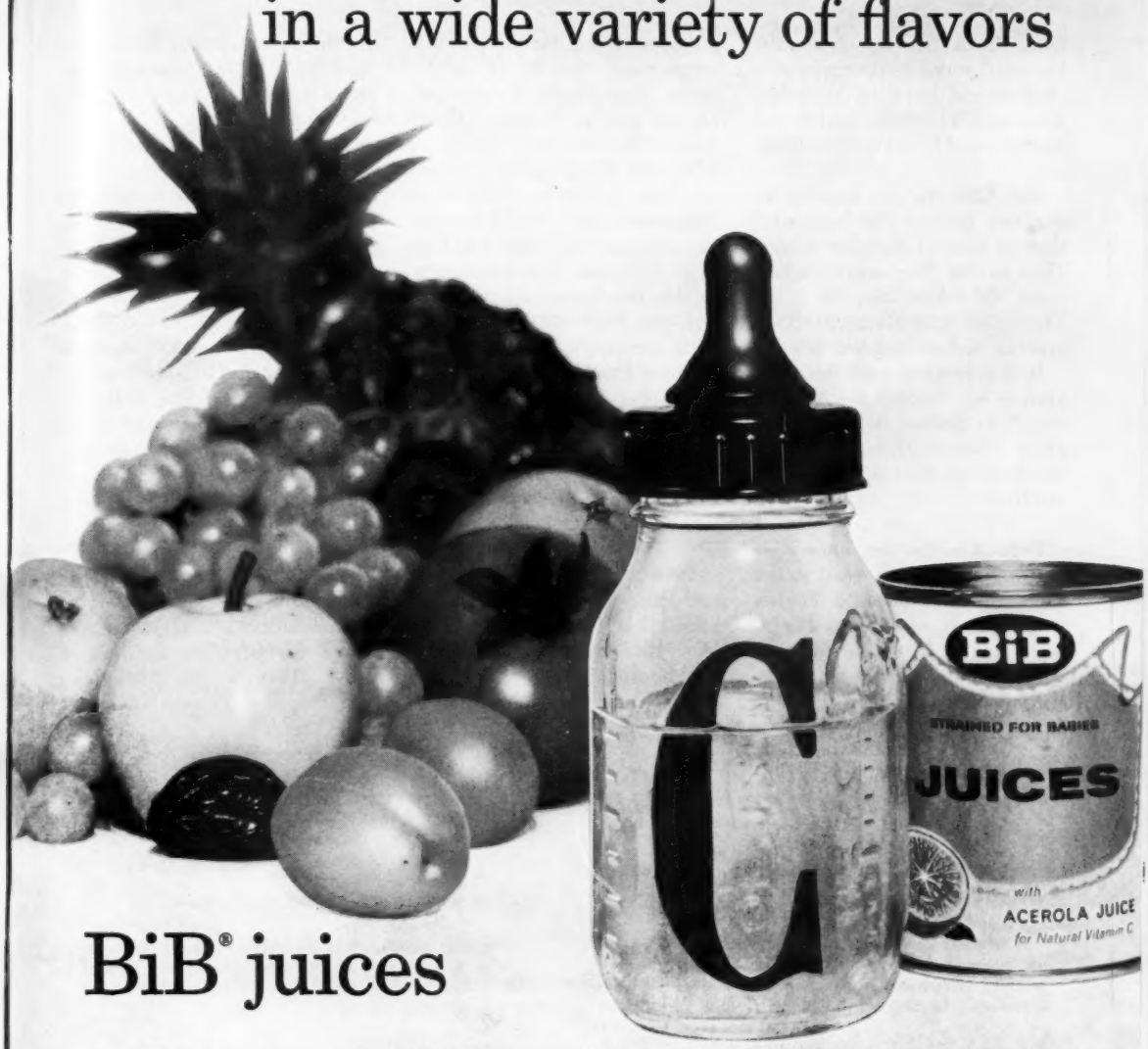
Feb. 21—To visit the bookstores and lunching at the Samaritaine, and in the afternoon with Delafresnaye of the Council of International Organizations of the Medical Sciences. An advanced symposium on immunology will be held in Monaco in May. In the evening to dine at L'Espadon and then to a spectacle called "La Nouvelle Eve." Completed the reading of Noel Coward's "Pomp and Circumstance," which has the flavor of vintage Wodehouse and is in many particulars funnier.

Feb. 22—All day editing the discussions of the proceedings of the first International Congress on Congenital Malformations, which is replete with innumerable suggestions for new investigations in this exciting field. In the evening reading with Mistress Pepys, who fights a cold. Reading now "The Hunter," by Tuviah Friedman, which tells of his 15 year search for Adolf Eichmann and is horrifying with its record of Nazi cruelties.

Feb. 23—At noon leaving Paris in a great fog for a good trip to London in a BEA Viscount, Mistress Pepys being weak from her influenza. To our rooms at Claridge's came the Runyons, who told a dramatic tale of their complicated flight to London during the airline engineers' strike. After dining sumptuously in the

(Continued on page A-166)

NOW...high natural vitamin C in a wide variety of flavors



BiB® juices

Acerola–Exclusive BiB Feature:

All BiB juices—Orange, Apple, White Grape, Pineapple, Prune-Orange, Orange-Apricot, and Tomato—are standardized to protective vitamin C levels with Acerola, the richest known *natural* source of vitamin C.[1,2] Each ounce of *all* BiB juices—citrus or non-citrus—provides more than the minimum daily requirement of vitamin C for infants.

BiB Orange Juice–Hypoallergenic

Hypoallergenicity and improved tolerance are achieved through special processing which reduces the seed protein and peel oil content to negligible quantities. In a clinical study with Acerola, "No reactions occurred from ingestion or from skin and intradermal tests with Acerola juice."[2]

A Wide Variety at an Early Age

BiB juices permit early introduction of a wide variety of flavors—valuable in taste-training the infant. Special process assures free flow through bottle nipple; ideal for spoon or cup feeding, too. BiB juices require no reconstitution, no heating, no defrosting. All mother does is open the can of BiB juice and it's ready for feeding.

References: (1) Asenjo, C. F., and Freire de Guzman, A. R.: Science *103*:219 (Feb. 22) 1946. (2) Clein, N. W.: J. Pediat. *48*:140-145 (Feb.) 1956.

Edward Dalton Co.
A DIVISION OF
MEAD JOHNSON & COMPANY

Quality products from nutritional research

45461

hotel, began "The Agony and the Ecstasy," which is Irving Stone's biographical novel of Michelangelo and Florence under the Medicis, and found it enthralling.

Feb. 24—In the morning to see my friend Farbey, who showed some Georgian silver. Then to the *Practitioner*, where were Mike Fletcher, W. A. R. Thomson and General Hargreaves, and we lunched later.

In the evening with the Runyons to see "A Man for All Seasons," by Robert Bolt, which is about Thomas More, Cromwell, the Duke of Norfolk, and Richard Rich.

Feb. 25—To the library of the Royal Society to read in the magazines, and then to Foyle's until William and Susan Benjamin came to lunch. In the evening to the Berkeley Hotel, where Milton and Laura Runyon entertained at dinner for their twelfth anniversary. Old Pepys sat between Mrs. Philip Youngman-Carter, who is Margery Allingham, a famous writer of mystery tales, and Miss Louisa Callender, who was a director of William Heinemann, Ltd., British publishing company. Opposite was Captain William Warwick, who guides the Queen Mary on its voyages. Here also were Evans of Heinemann's, who sat next to Mistress Pepys, and at her other side Robert Lusty of the Hutchinson and Company, Ltd., publishing house. Happy at seeing again Winifred Nerney, who was secretary to Arnold Bennett, and other ladies of the Doubleday office.

Feb. 26—Early to the airport and three hours later in Madrid amidst warm sunshine. So to the Hotel Ritz and then to walk along the boulevards, in particular looking into the shop windows on the José Antonio. In the evening with Edith Bulson to dine at El Bodega.

Feb. 27—Still reading Irving Stone's magnificent novel. To Anna Lise, *couturière*, who designs for Mistress Pepys. Next to Horcher's, and met there Dr. Henry Rapaport of Whitney Point, New York, with his lady. For dinner to the home of Edith Bulson, where came Dr. Martinez Alonzo, who has finished his autobiography; Dr. Bosch-Marin, medical head of the social security; Gomez de Molina, who represents Eli Lilly; the radiologist Moison; Margery Presley; and Martha Miles of New Orleans.

Feb. 28—To the Prado to see an exhibit of Velázquez for his three-hundredth anniversary and Goya, for here are the best of Goya. Then to the bibliotheca for a special Picasso exhibit.

The Medical Muse

RICHARD ARMOUR

WORDSWORTH REVISITED

A newly discovered drug, lycoramine, that is found in the bulbs of daffodils may prove effective in the treatment of myasthenia gravis, a neuromuscular disease.—*American Druggist.*

I wandered lonely as a cloud
Among the lovely hills,
And suddenly came on a crowd
Of golden daffodils.

My heart leapt up when I beheld
Those daffodils so gay.
I cried, as by a force compelled,
"This is my lucky day!

"I shall uproot these flowers I've found,
Though some may think me silly.
They'll bring at least a buck a pound
From Squibb or Eli Lilly!"

MAYBE THE BODY NEEDS IT, BUT—

Army tests indicate that the hotter it is, the more one needs to eat, because of increased blood flow, greater sweat gland activity, and loss of calories from sweat loss.—*News item.*

How often, in the summer's heat,
We mutter, "It's too hot to eat,"
And food on plates is left untasted
And carried out, completely wasted.

But if the army tests are right,
We should eat everything in sight
To strengthen blood flow, help us sweat,
And have lost calories offset.

It may be true, it may be not,
That we should eat more when it's hot,
But on a muggy day, no breeze,
Just try convincing taste buds, please.